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Health and Environmental Effects Profile for Naphthalene

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16. ABSTRACT

The Health and Environmental Effects Profile for Naphthalene was prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Solid Waste and Emergency Response to support listings of hazardous constituents of a wide range of waste streams under Section 3001 of the Resource Conservation and Recovery Act (RCRA) and to provide health-related limits for emergency actions under Section 101 of the Comprehensive Environmental Response, Compensation and Liability Act (CERCLA). Both published literature and information obtained from Agency program office files were evaluated as they pertained to potential human health, aquatic life and environmental effects of hazardous waste constituents.

Quantitative estimates have been presented provided sufficient data are available. Naphthalene has been determined to be a systemic toxicant. A Reference Dose (RfD), defined as an estimate (with uncertainty spanning perhaps an order of magnitude) of the daily exposure to the human population (including sensitive subgroups) that is likely to be without appreciable risk of deleterious effect during a lifetime, for naphthalene is 0.40 mg/kg/day for oral exposure.

The Reportable Quantity (RQ) value of 1, 10, 100, 1000 or 5000 pounds is used to determine the quantity of a hazardous substance for which notification is required in the event of a release as specified by CERCLA based on chronic toxicity. The RQ value for naphthalene is 1000.

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HEALTH AND ENVIRONMENTAL EFFECTS PROFILE FOR NAPHTHALENE

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PREFACE

Health and Environmental Effects Profiles (HEEPs) are prepared for the Office of Solid Waste and Emergency Response by the Office of Health and Environmental Assessment. The HEEPs are intended to support listings of hazardous constituents of a wide range of waste streams under Section 3001 of the Resource Conservation and Recovery Act (RCRA), as well as to provide health-related limits for emergency actions under Section 101 of the Comprehensive Environmental Response, Compensation and Liability Act (CERCLA). Both published literature and information obtained from Agency program office files are evaluated as they pertain to potential human health, aquatic life and environmental effects of hazardous waste constituents. The literature searched and the dates of the searches are included in the section titled "Appendix: Literature Searched." The literature search material is current through November, 1985.

Quantitative estimates are presented provided sufficient data are available. For systemic toxicants, these include Reference doses (RfDs) for chronic exposures. An RfD is defined as the amount of a chemical to which humans can be exposed on a daily basis over an extended period of time (usually a lifetime) without suffering a deleterious effect. In the case of suspected carcinogens, RfDs are not estimated in this document series. Instead, a carcinogenic potency factor of q_1^* (U.S. EPA, 1980) is provided. These potency estimates are derived for both oral and inhalation exposures where possible. In addition, unit risk estimates for air and drinking water are presented based on inhalation and oral data, respectively.

Reportable quantities (RQs) based on both chronic toxicity and carcinogenicity are derived. The RQ is used to determine the quantity of a hazardous substance for which notification is required in the event of a release as specified under CERCLA. These two RQs (chronic toxicity and carcinogenicity) represent two of six scores developed (the remaining four reflect ignitability, reactivity, aquatic toxicity and acute mammalian toxicity).

The first draft of this document was prepared by Syracuse Research Corporation under EPA Contract No. 68-03-3228. The document was subsequently revised after reviews by staff within the Office of Health and Environmental Assessment: Carcinogen Assessment Group, Reproductive Effects Assessment Group, Exposure Assessment Group, and the Environmental Criteria and Assessment Office in Cincinnati.

The HEEPs will become part of the EPA RCRA and CERCLA dockets.

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The initial draft of this report was prepared by Syracuse Research Corporation under Contract No. 68-03-3228 for U.S. EPA's Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH. Dr. Christopher DeRosa was the Technical Project Monitor and Helen Ball was the Project Officer. The final documents in this series were prepared for the Office of Solid Waste, Washington, DC.

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EXECUTIVE SUMMARY

Naphthalene is a white solid with a characteristic mothball odor at ambient temperature. It is almost insoluble in water but is soluble in a variety of organic solvents (Windholz, 1983). As of January 1985, the annual U.S. production capacity for this chemical was 435 million pounds. Currently, five U.S. companies at six manufacturing sites produce naphthalene (SRI, 1985). The total U.S. production of crude naphthalene in 1982 was 230 million pounds (USITC, 1983). Napthalene is produced mainly from coal tar and petroleum fractions (SRI, 1985). It is used as an intermediate for making dyes; in the manufacture of synthetic resins, celluloid, lampblack and smokeless powder; as an intermediate for the manufacture of solvents and lubricants; and as a moth repellent and insecticide (Windholz, 1983).

The most significant fate process for naphthalene in the atmosphere is likely to be its reaction with HO radical. From the measured rate constant in the range of 1.6×10^{-11} to 2.42×10^{-11} cm^3 $molecule^{-1}$ sec^{-1} (Lorenz and Zellner, 1983; Atkinson et al., 1984a) at 25°C and the average atmospheric HO radical concentration of 10^6 molecules cm^{-3} (Cupitt, 1980), the half-life of naphthalene that is due to its reaction with HO radical has been estimated to be 8-12 hours. In photochemical smog systems, NO_3 radical formed at an average concentration of 2×10^9 molecule cm^{-3} (Atkinson et al., 1984b) can react with naphthalene having a rate constant of 6.4×10^{-15} cm^3 $molecule^{-1}$ sec^{-1} (Atkinson et al., 1984b); the estimated half-life for this reaction is 15 hours. Although no experimental data is available, naphthalene's physical properties suggest that significant removal of atmospheric naphthalene through physical processes (wet and dry deposition etc.) are unlikely.

The two most important processes likely to remove naphthalene from water are volatilization and biodegradation (Lee et al., 1972; Herbes et al., 1980; Rodgers et al., 1983). The volatilization half-life of naphthalene at a current velocity of 0.1 m/sec and a wind velocity of 2 m/sec was estimated to be 60 hours, while the half-life was estimated to be 5 hours at a current velocity of 1 m/sec and a wind velocity of 3 m/sec (Southworth, 1979). Herbes et al. (1980) predicted the contributions of different processes in the removal of naphthalene from water in a shallow, rapidly flowing stream as follows: photolysis, <1%; microbial degradation, 4.4%; sediment sorption, 15.5%; and volatilization, 80%. The overall half-life of naphthalene in river water was experimentally determined to be 2.3 days (Zoeteman et al., 1980). The BCF of naphthalene in aquatic organisms, determined through correlation equations and by experimental methods, indicate values in the range of 20-90 (Kenaga, 1980; Roubal et al., 1978; Lee, 1977b; Hansen et al., 1978). When exposed to naphthalene-contaminated water for 16 days, the BCF value in the bile of trout, Salmo gairdneri, was reported to be 19,200 (Lech and Bend, 1980). All the studies indicate that naphthalene will not significantly bioaccumulate in edible portions of aquatic organisms.

Biodegradation and volatilization from soil surfaces are the two important processes for the removal of naphthalene from soil (Schwarzenbach et al., 1983; Bouwer et al., 1984; Jury et al., 1984). The estimated volatilization half-lives for naphthalene from a soil containing 1.25% organic carbon were as follows: 1.1 day from soil 1 cm deep and 14 days from soil 10 cm deep (Jury et al., 1984). The overall half-life of naphthalene in soil from a waste disposal site was estimated to be 3.6 months (Zoeteman et al., 1981). Therefore, contamination of groundwater by naphthalene is likely to occur from waste disposal sites.

Naphthalene has been detected in ambient air in the United States and other parts of the world. The median concentrations of naphthalene in U.S. urban/suburban and source-dominated atmospheres were 940 and 2100 ng/m³, respectively (Brodzinsky and Singh, 1982). Based on these values and a human air inhalation rate of 20 m³/day, the daily exposures to atmospheric naphthalene have been estimated to be 18.8 and 42 µg, respectively.

Naphthalene has been detected in wastewater, urban runoff water, surface waters and groundwater from contaminated sites. For example, naphthalene concentrations in the wastewater of a speciality chemical plant were reported to range from 1-4 mg/ℓ (Jungclaus et al., 1978). Naphthalene at a concentration of 1.8 mg/ℓ was reported in groundwater near an underground coal gasification site in northeastern Wyoming (Stuermer et al., 1982). Naphthalene has been detected in drinking water samples in the United States and elsewhere in the world. The concentration of naphthalene in a District of Columbia drinking water was reported to be 1 µg/ℓ (Scheiman et al., 1974). In Ottawa, Canada, tap water, Benoit et al. (1979) detected naphthalene in the concentration range of 4.8-6.8 ng/ℓ. Grob and Grob (1974) reported a naphthalene concentration of 8 ng/ℓ in tap water from Zurich, Switzerland. The human exposure to naphthalene from drinking water in the United States cannot be estimated unless additional monitoring data become available.

Several food items have been reported to contain naphthalene. The concentration of naphthalene in mussels, Mytilus edulis and M. californian, may be as high as 96 µg/kg (dry wt.) (Galloway et al., 1983). A naphthalene concentration of 22 µg/kg (dry wt.) was reported in smoked Japanese horse mackeral (Fazio and Howard, 1983). Pellizzari et al. (1982) detected naphthalene in 6/12 samples of mothers' milk collected from three states in

the United States. Human exposure to naphthalene from ingestion of foods cannot be estimated unless composite levels of naphthalene in foods from market basket surveys are available.

The lowest reported LC_{50} values for freshwater and saltwater fishes were 0.11 mg/ℓ for rainbow trout larvae (Black et al., 1983) and 1.2 mg/ℓ for pink salmon (Moles et al., 1981), respectively. The lowest reported LC_{50} value for freshwater invertebrates was 1 mg/ℓ for dragonfly, Somatochlora singulata, larvae (Correa and Coler, 1983) and Daphnia pulex (Trucco et al., 1983). Among saltwater invertebrates, larval crustaceans appeared to be the most sensitive to naphthalene, with 0.008-0.012 mg/ℓ causing 100% mortality of spot shrimp and dungeness crab larvae (Sanborn and Malins, 1977). Limited chronic and subchronic toxicity data did not indicate lower thresholds for toxicity than the acutely toxic levels in the most sensitive species.

The lowest concentration that caused clearly adverse effects on aquatic plants was 0.4 mg/ℓ, which caused a 50% reduction in growth of the marine alga Skeletonema costatum (Oestgaard et al., 1984).

Data concerning naphthalene residues in aquatic biota indicated that naphthalene does not bioaccumulate to a great extent in most species. In general, naphthalene appeared to be metabolized and eliminated rapidly.

Absorption of naphthalene in man and animals has been demonstrated by oral and inhalation exposure (Chusid and Fried, 1955; Zuelzer and Apt, 1949; Nash, 1903; Gross et al., 1958; Haggerty, 1956; Valaes et al., 1963; Sandmeyer, 1981). Its oral absorption may be enhanced by solution in oil or ingestion in water rather than in food. Naphthalene has been shown to distribute in a wide variety of tissues of several species following absorption (Lawler et al., 1978; Eisele, 1985). Highest levels appear in the

liver, kidneys and lungs of most species tested. Levels in fat are variable and not consistent. In treated swine, levels are high in fat after a single treatment, but higher in liver and lower in fat after treatment for 31 days (Eisele, 1985). While naphthalene itself has not been identified in the urine after absorption, its metabolites have been identified in humans, rats and mice (Mackell et al., 1951; Horning et al., 1980; Stillwell et al., 1978, 1979, 1980). Naphthalene is first converted to naphthalene1,2-oxide in the liver by a cytochrome P-450-dependent monooxygenase (Jerina et al., 1968, 1970). The reactive epoxide is converted to other oxidation products and is detoxified by conjugation with glutathione (Boyd et al., 1972). In the rat, glutathione conjugation is a major metabolic pathway (Chen and Dorough, 1979; Summer et al., 1979), but this pathway appears to be insignificant in primates (Rozman et al., 1982; Summer et al., 1979). Naphthalene dihydrodiol released from the liver can be converted in the eye to 1,2-napthoquinone, causing toxic reactions such as cataracts (Van Heyningen and Pirie, 1966, 1967; Rees and Pirie, 1967; Van Heyningen, 1979). Reactive metabolites from the cytochrome P-450-mediated metabolism of naphthalene in the liver have also been shown to deplete pulmonary glutathione and become covalently bound to tissue macromolecules, resulting in damage to the bronchiolar epithelium (Buckpitt and Warren, 1983; Buckpitt, 1982, 1983). Rats treated with intraperitoneal ^{14}C-naphthalene excreted 24% of the dose of radioactivity in the urine by 24 hours and 60% in the urine by 72 hours. By 72 hours, 14% of the dose of radioactivity had been recovered from the feces.

Knake (1956) reported increased incidence of lymphosarcomas in rats injected with 500 mg/kg coal tar naphthalene every 2 weeks for 7 treatments; however, the injection site was painted with a carcinogen (carbolfuchsin)

and the naphthalene was known to contain impurities. In another study, Knake (1956) painted mice with a 0.5% solution of coal tar naphthalene and reported an increased incidence of lymphatic leukemia. Again, the coadministration of carcinogenic impurities cannot be discounted.

Schmahl (1955) observed no tumors in BDI and BDII rats fed naphthalene in doses of 10-20 mg/day 6 days/week up to a total dose of 10 g/rat for 700 days, or in rats receiving a single intraperitoneal or subcutaneous dose of 20 mg/rat/week for 40 weeks. An increase in the number or size of γ-GT positive foci was not observed in the livers of rats exposed to naphthalene after partial hepatectomy (Tsuda et al., 1980). Naphthalene is currently being tested by the National Toxicology Program (mice, inhalation exposure), but final results are not available and histopathology is currently in progress (NTP, 1985). Data are inadequate to access the carcinogenic potential for naphthalene.

Naphthalene was found to be nonmutagenic in a variety of microsomal/bacterial assay systems (see Table 5-1) (McCann et al., 1975; Seixas et al., 1982; Anderson and Styles, 1978; Kaden et al., 1979; Mamber et al., 1983; Sina et al., 1983; Mortelmans et al., 1986). Naphthalene was negative for transformation activity and tumorigenicity when tested *in vitro* using rat and mouse cells pretreated with leukemia virus (Freeman et al., 1973; Rhim et al., 1974).

Results of available teratogenicity reports are summarized in Table 5-2 and are somewhat unclear. Matorova and Chetverikova (1981) reported no visible or microscopic anomalies at 0.075 mg/kg, but embryonic and preimplantation mortality was significantly higher and subcutaneous hematomas were observed on the spine and extremities at $\geq$0.15 mg/kg. Plasterer et al. (1985) reported reduced numbers of live young at parturition, probably

because of early embryonic mortality in mice treated during gestation with 300 mg/kg/day. Coworkers at one laboratory (Harris et al., 1979; Hardin et al., 1981) report both no evidence of fetal or maternal toxicity in the latter publication and progeny with retarded cranial ossification and heart development in the former publication when an intraperitoneal dose of 395 mg/kg naphthalene was given on days 1-15 of gestation to female Sprague-Dawley rats.

Naphthalene or its metabolites apparently can cross the placenta in humans in amounts sufficient to cause fetal toxicity (U.S. EPA, 1980a; Bergheim et al., 1973). Hemolytic anemia has been observed in infants whose mothers were exposed to naphthalene during pregnancy (Zinkham and Childs, 1958; Anziulewicz et al., 1959).

The NTP has investigated the subchronic toxicity of naphthalene in 13-week studies in rats (NTP, 1980a) and mice (NTP, 1980b). In rats, mortality, frank signs of toxicity, lesions in the kidneys and thymus, and signs of anemia occurred at 400 mg/day, mild kidney lesions occurred at 200 mg/kg (lower dose groups were not examined histologically) and body weight gain depression occurred in males at 200 and females at 100 mg/kg. No adverse effects occurred at $\leq$50 mg/kg. In mice, frank but transient signs of toxicity occurred only at 200 mg/kg, the highest dose tested. No signs of toxicity occurred at 100 mg/kg and no compound-related histopathological lesions were observed at 200 mg/kg, the only treatment group histopathologically examined. In both the rat and mice studies, treatments were given 5 days/week.

When naphthalene was administered by gavage to male and female CD-1 mice for 90 days at doses of 5.4, 53 and 133 mg/kg/day, no compound-related mortality or changes in body weights were observed (Shopp et al., 1984).

Absolute and relative spleen weights were reduced in female mice at the high dose only, but no changes in organ weights were observed in the males. No compound-related effects were observed on serum enzymes and electrolyte levels or immunological screening tests. There was no evidence of compound-induced hemolytic anemia, cataract formation, lung damage or other pathological effects. A significant decrease in hepatic microsomal aryl hydrocarbon hydroxylase was observed in both sexes.

Schmahl (1955) reported no compound-related effects on mortality, histopathology, tumor formation, eye damage or signs of toxicity in BDI and BDII rats administered naphthalene orally at doses of 10-20 mg/day, 6 days/week for 700 days. The rats were observed until spontaneous death, and the average lifespan was 800 days.

Several short-term animal studies reported cataract development as a result of naphthalene administration (Ghetti and Mariani, 1956; Van Heyningen and Pirie, 1976; Fitzhugh and Buschke, 1949). Naphthalene has been associated with cataract formation (Lezenius, 1902; Ghetti and Mariana, 1956) and anemia (U.S. EPA, 1980a; Harden and Baetjer, 1978) in humans.

An RfD (ADI) of 0.4 mg/kg/day or 28.0 mg/day for a 70 kg human, was derived by application of an uncertainty factor of 100 to the chronic NOEL of 40.1 mg/kg/day estimated from the TWA based on a total dose of 10 g/rat (10-20 mg/rat/day) in the 700-day experiment by Schmahl (1955). A CS of 13.2, associated with an RQ of 1000, was based on the development of mild histopathological lesions in rats intubated 5 days/week for 13 weeks at 200 mg/day (NTP, 1980a).

Data are inadequate to access the carcinogenic potential for naphthalene. The chemical is classified as an IARC Group 3 and U.S. EPA Group D compound.

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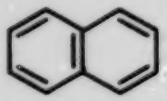
LIST OF ABBREVIATIONS

ADI	Acceptable daily intake
ATP	Adenosine triphosphate
BCF	Bioconcentration factor
CAS	Chemical Abstract Service
CS	Composite score
EC_{50}	Concentration effective to 50% of recipients
γ-GT	γ-Glutamyl transpeptidase
K_{oc}	Soil sorption coefficient
K_{ow}	Octanol/water partition coefficient
LC_{50}	Concentration lethal to 50% of recipients
LOAEL	Lowest-observed-adverse-effect level
MATC	Maximum acceptable toxicant concentration
MED	Minimum effective dose
NADH	Nicotinamide adenine dinucleotide (reduced form)
NOAEL	No-observed-adverse-effect level
NOEC	No-observed-effect concentration
NOEL	No-observed-effect level
ppm	Parts per million
RQ	Reportable quantity
RV_d	Dose-rating value
RV_e	Effect-rating value
STEL	Short-term exposed level
TLV	Threshold limit value
TWA	Time-weighted average

1. INTRODUCTION

1.1. STRUCTURE AND CAS NUMBER

The chemical commonly called naphthalene is also known as moth balls, camphor tar, naphthene and albo carbon (U.S. EPA, 1985). The structure, empirical formula, molecular weight and CAS Registry number for naphthalene are as follows:



Empirical formula: $C_{10}H_8$

Molecular weight: 128.16

CAS Registry number: 91-20-3

1.2. PHYSICAL AND CHEMICAL PROPERTIES

Naphthalene is a white solid with a characteristic mothball odor at ambient temperature. It is almost insoluble in water, but is soluble in benzene, toluene, ether and several other organic solvents (Windholz, 1983). The relevant physical properties of naphthalene are listed below:

Melting point:	80.2°C	Verschueren, 1983
Boiling point:	217.9°C (sublimes)	Verschueren, 1983
Density 20/4°C:	1.162	Windholz, 1983
Flash point (open cup):	79°C	Windholz, 1983
(closed cup):	88°C	Windholz, 1983
Vapor pressure at 25°C:	0.082 mm Hg	Hine and Mookerjee, 1975; Mackay et al., 1982
	0.088 mm Hg	Mackay et al., 1979
Water solubility: at 25°C	31.7 mg/ℓ	May et al., 1978; Kenaga, 1980
Henry's Law Constant: at 25°C	4.83×10^{-4} atm-m³/mol	Mackay et al., 1979
	5.53×10^{-4} atm-m³/mol	Southworth, 1979

Log K_{ow}:	3.01-4.70	Garten and Trabalka, 1983
	3.30 (recommended)	Hansch and Leo, 1985
Log K_{oc}:	2.75-4.16 (for % org. carbon of 14%-33%)	Southworth and Keller, 1984
	3.11 (for 3% org. carbon)	Karickhoff et al., 1979
	2.98-3.5 (for 0.71%-2.1% org. carbon)	Karickhoff, 1980
Air odor threshold:	0.084 ppm	Amoore and Hautala, 1983
Water odor threshold:	0.021 ppm	Amoore and Hautala, 1983
Conversion factor at 20°C:	1 ppm = 5.24 mg/m³ 1 mg/m³ = 0.191 ppm	

Naphthalene, like other aromatic compounds, undergoes electrophilic substitution reactions. It also undergoes oxidation with strong oxidizing agents to form naphthoquinone and then phthalic acid or phthalic anhydride, depending on reaction conditions. Naphthalene also undergoes catalytic hydrogenation to form tetralin (Gutsche and Pasto, 1975). None of these reactions, however, is environmentally significant.

1.3. PRODUCTION DATA

According to U.S. EPA (1977), 15 U.S. companies at 23 different sites manufactured this chemical in 1977. As of January 1985, the following companies, with their annual capacities, produced this chemical in the United States.

Producer and Location	Annual Capacity (millions of pounds)
Allied Corp, Ironton, OH	75
Chem. Exchange Indust., Inc., Baytown, TX	30
DuPont Co., Chocolate Bayou, TX	90
Kopper Co., Inc., Cicero, IL	30
Follansbee, WV	150
Texaco, Inc., Delaware City, DE	60
TOTAL	435

The total U.S. production of crude naphthalene in 1982 was 230 million pounds (USITC, 1983); more recent production data are not available because of confidentiality. Naphthalene is produced mainly from coal tar and petroleum fractions (SRI, 1985).

1.4. USE DATA

Naphthalene is used in the manufacture of phthalic and anthranilic acids, which are used in making dyes. Naphthols, naphthylamines and sulfonic acid derivatives derived from naphthalene are also used in the manufacture of dyes. Naphthalene is used in the manufacture of synthetic resins, celluloid, lampblack and smokeless powder. Tetralin and decalin obtained from hydrogenation of naphthalene are used as solvents, in lubricants and in motor fuels. Naphthalene is used directly as a moth repellant and insecticide (Windholz, 1983). It is also used as antihelmintic, vermicide and an intestinal antiseptic (U.S. EPA, 1980a).

1.5. SUMMARY

Naphthalene is a white solid with a characteristic mothball odor at ambient temperature. It is highly insoluble in water but is soluble in a variety of organic solvents (Windholz, 1983). As of January 1985, the annual U.S. production capacity for this chemical was 435 million pounds. Currently, five U.S. companies at six manufacturing sites produce naphthalene (SRI, 1985). The total U.S. production of crude naphthalene in 1982 was 230 million pounds (USITC, 1983). Napthalene is produced mainly from, coal tar and petroleum fractions (SRI, 1985). It is used as an intermediate for making dyes; in the manufacture of synthetic resins, celluloid, lampblack and smokeless powder; as an intermediate for the manufacture of solvents and lubricants; and as a moth repellent and insecticide (Windholz, 1983).

2. ENVIRONMENTAL FATE AND TRANSPORT PROCESSES

2.1. AIR

The fate of naphthalene in the atmosphere with respect to direct photolysis has not been comprehensively studied. In sunlight, naphthalene absorbs wavelengths in the region from 288-330 nm (Zadelis and Simmons, 1983). The disappearance quantum yield of naphthalene in aqueous solution at 313 nm has been measured at 0.015 (Zadelis and Simmons, 1983; Zepp and Schlotzhauer, 1979). The photolysis data for naphthalene in aqueous solution may be of little significance, however, if naphthalene is present in the atmosphere in the particle-sorbed phase, since particle size, porosity and the nature of particles may dictate the photolysis rate in the adsorbed state and may vary considerably from photolysis in solution phase (Santodonato et al., 1981). It is likely that naphthalene will remain in the vapor phase in the atmosphere (Eiceman and Vandiver, 1983; Pitts et al., 1985) and the photolysis of naphthalene in the solution phase may be comparable to its atmospheric photolysis. The half-life for direct solar photolysis of naphthalene in aqueous solution has been estimated as 71 hours (Zepp and Schlotzhauer, 1979). Therefore, the half-life for direct solar photolysis of naphthalene in the atmosphere is likely to be ~3 days.

Lorenz and Zellner (1983) determined the rate constant for the gas-phase reaction of HO radical with naphthalene over the temperature range of 64-252°C; a rate constant at 21°C can be obtained from the extrapolation of these values, yielding 1.6×10^{-11} cm^3 $molecule^{-1}$ sec^{-1} (Atkinson et al., 1984a). A similar rate constant at 21°C was also determined experimentally by Atkinson et al. (1984a) as 2.42×10^{-11} cm^3 $molecule^{-1}$ sec^{-1}. Assuming an average atmospheric HO radical concentration of 1×10^6 molecule cm^{-3} (Cupitt, 1980), the half-life of naphthalene that is due to its reaction with HO radical can be estimated to be 8-12 hours.

The gas-phase reaction of naphthalene with O_3 was also studied by Atkinson et al. (1984a). At an O_3 concentration of 9×10^{13} molecule cm^{-3}, no loss of naphthalene was observed over a period of 145 minutes. The upper limit of the rate constant for this reaction at 21°C was $<2 \times 10^{-19}$ cm^3 $molecule^{-1}$ sec^{-1} (Atkinson et al., 1984a). Assuming an average atmospheric O_3 concentration of 1×10^{12} molecule cm^{-3} (Graedel, 1978), the half-life for this reaction is >40 days; therefore, this reaction is not significant in determining the atmospheric fate of naphthalene. The rate constant for N_2O_5 reaction with naphthalene in the atmosphere at 25°C was reported by Pitts et al. (1985) to be $(2\text{-}3) \times 10^{-17}$ cm^3 molecule sec^{-1}. The atmospheric N_2O_5 concentration at night typically ranges between $\sim 2.4 \times 10^7$ and $\sim 2.4 \times 10^{11}$ molecule cm^{-3}. During daylight hours, the concentration of N_2O_5 is negligible because of rapid photolysis (Pitts et al., 1985). Pitts et al. (1985) combined the time-concentration profiles of N_2O_5 with its reaction rate constant with naphthalene and estimated a half-life for this reaction in the atmosphere to be ≥ 7 days. Therefore, this reaction is not likely to be a significant atmospheric fate determining process.

Nitrate radicals ($NO_3 \cdot$) are formed in photochemical smog systems from the reaction of O_3 with NO_2 according to the following reaction: $O_3 + NO_2 \rightarrow NO_3 + O_2$ (Carter et al., 1981).

The rate constant for NO_3 radical reaction with naphthalene in the air at 25°C was studied by Atkinson et al. (1984b). Assuming an atmospheric NO_3 radical concentration of 2×10^9 molecule cm^{-3} and the reported rate constant of 6.4×10^{-15} cm^3 $molecule^{-1}$ sec^{-1} (Atkinson et al., 1984b), the atmospheric half-life of naphthalene that is due to its reaction with NO_3 radical is estimated to be 15 hours. Thus, this reaction rate is slower than naphthalene reaction with HO radical in the atmosphere.

The transport and removal of naphthalene through commonly occurring atmospheric physical processes have not been comprehensively studied. Based on its physical properties and certain experimental observations, however, it is possible to predict its atmospheric transport patterns. Since naphthalene is likely to be present in the gas phase in the atmosphere (Eiceman and Vandiver, 1983; Pitts et al., 1985), and since it is highly insoluble in water, the removal of atmospheric naphthalene through dissolution into raindrops or entrapment by snow and subsequent precipitation may not be a significant process. Removal of vapor-phase naphthalene through adsorption onto atmospheric aerosol particles and subsequent precipitation is not likely to be a significant process, according to the estimation method of Cupitt (1980). Since the saturation vapor pressure of naphthalene is $>10^{-7}$ mm Hg, removal of atmospheric naphthalene by sorption upon impaction at the surface of earth or bodies of water will occur but is not likely to be significant compared with its chemical removal mechanisms.

2.2. WATER

The abiotic chemical processes of naphthalene in water have been studied less than its biodegradation processes. The rate constants for naphthalene reaction with singlet oxygen ($^1O_2$) and peroxy radical ($RO_2\cdot$) have been estimated to be <360 and <1 M^{-1} $hour^{-1}$, respectively (Mabey et al., 1981). Combining these rate constant values with the expected $^1O_2$ and RO_2 radical concentrations in surface waters of 10^{-12} and 10^{-9} M, respectively (Mill et al., 1980), the half-lives for these two reactions can be estimated to be extremely high. Therefore, neither of these reactions are expected to significantly affect the fate of naphthalene in water. Zepp and Schlotzhauer (1979), from the measured quantum yield value of naphthalene at 313 nm, estimated that the half-life for direct photolysis near

the surface of bodies of water by midday, midsummer solar radiation at a latitude of 40°N was 71 hours. As a result of light attenuation, the direct photolysis half-life in a 5 m deep inland water body was estimated to be 550 days (Zepp and Schlotzhauer, 1979). It was also reported (Zepp and Schlotzhauer, 1983) that certain green and blue-green algae accelerate the solar photoreaction of naphthalene by a factor of 1.3-2.7. The first-order photolytic rate constant for naphthalene was also predicted from EXAMS and SLSA modeling (Rodgers et al., 1983). The estimated rate constant by this method was reported to be 0.005 $hour^{-1}$. Therefore, the half-life for photolysis can be estimated to be ~140 hours, a value about twice that reported by Zepp and Schlotzhauer (1979).

The biodegradation potential for napnthalene has been extensively studied. The degradation of naphthalene by pure cultures of microorganisms under aerobic conditions has been reported by several investigators (Cerniglia et al., 1979, 1980a,b, 1982; Laborde, 1979; Mulkins-Phillips and Stewart, 1974; Dean-Raymond and Bartha, 1975; Ferris et al., 1973; Fedorak et al., 1984; Bhosle and Mavinkurve, 1980; Groenewegen and Stolp, 1976; McKenna, 1976; Jeffrey et al., 1975). A review of the different species of microorganisms that are capable of degrading naphthalene is given by Givson (1977) and Kobayashi and Rittman (1982). Although the studies with pure cultures of microorganisms establish the potential for biodegradability of organics and the specific mechanistic biodegradation pathways with a specific microorganism, these studies are not useful in predicting the rate of biodegradation of a chemical in natural water. The degradation of naphthalene with mixed microorganisms has also been studied quite extensively. Mixed microorganisms isolated from soil (Herbes et al., 1977), from settled domestic wastewater (Herbes at al., 1977; Tabak et al., 1981a,b), from Bay water (Walker and Colwell, 1975), and from sediments (Herbes and Schwall,

1978; Hambrick et al., 1980; Schwall and Herbes, 1979; Bauer and Capone, 1985) show that naphthalene is readily biodegradable. The Japanese MITI test procedure that uses active sludge as a microbial inoculum to study the biodegradability of a test compound, which is determined by its biological oxygen demand, found naphthalene to be >74% degraded in 28 days (Yoshida et al., 1983). The results of the above studies and other studies (Meyer et al., 1984; Delaune et al., 1980; Cooney et al., 1985; Lee and Ryan, 1976) strongly suggest that the biodegradation of naphthalene is enhanced by the acclimation of the microorganisms; the biodegradability of naphthalene is temperature-dependent, degradation being less at temperatures <10°C than at temperatures >10°C; the presence of nutrients in bodies of water is important for the biodegradation of naphthalene; the biodegradation of naphthalene is concentration-dependent [unlike many aromatic hydrocarbons that show a linear decrease in degradation rates with increases in concentrations, the degradation rate of naphthalene increased with increases in aqueous concentration up to a certain level (130 µg/ℓ)]. Also, both pH and redox potential of the bodies of water are important in determining the biodegradation rate; the highest biodegradation may occur at pH 8 and the lowest at pH 5. Similarly, oxidized media (positive redox potential) enhance biodegradation compared with reduced media (negative redox potential). The presence of interfering compounds may inhibit the biodegradation potential of naphthalene. For example, naphthalene degraded rapidly alone but did not metabolize in the presence of phenol.

The biodegradation of naphthalene in sediment and water samples from a stream near a coal-coking treated wastewater discharge was reported by Herbes et al. (1980) and Herbes (1981). The half-life of naphthalene was estimated to be 3-9 hours in the sediment sample and 3-9 days in the water sample. The degradation of naphthalene in inshore, offshore and Gulf Stream

waters was studied by Lee and Ryan (1976), Lee (1977b) and Harris et al. (1977). The degradation rates of naphthalene in these waters varied from 0.05-4.4 µg/ℓ/day, corresponding to a half-life of 21-350 days. Naphthalene degraded more rapidly in the inshore water than in the offshore and Gulf stream waters. The biodegradability of naphthalene was also studied in a controlled ecosystem enclosure study by Lee et al. (1978). In seawater, up to 5% of the naphthalene was found to biodegrade daily. The first-order rate constant for naphthalene biodegradation was estimated to be 0.006 $hour^{-1}$ from the EXAMS and SLSA models (Rodgers et al., 1983); from this predicted biotransformation rate constant, the biodegradation half-life can be estimated to be ~5 days.

The rate of volatilization of naphthalene from water has been reported by several investigators. From an equation based on the liquid-phase mass transfer coefficient, Mackay and Leinonen (1975) estimated the half-life for evaporation of naphthalene in an aqueous solution 1 m deep to be 7.2 hours. The equation for estimating the volatilization half-life of naphthalene from both gas and liquid-phase mass transfer coefficients has been reported by Smith et al. (1981). Southworth (1979) estimated the effect of current and wind velocity on the rate of evaporation of naphthalene from bodies of water. It was estimated that a 10-fold increase in current velocity (0.1-1.0 m/sec) increased the predicted volatilization rate of naphthalene ~7.5 times; a 10-fold increase in wind velocity (1-10 m/sec) produced a 2- to 3-fold increase in volatilization rate. The half-life of naphthalene at a current velocity of 0.1 m/sec and a wind velocity of 2 m/sec was estimated to be 60 hours, while the half-life was estimated to be 5 hours at a current velocity of 1 m/sec and a wind velocity of 3 m/sec (Southworth, 1979). The first-order volatilization rate constant of naphthalene from

aquatic systems was also estimated from EXAMS modeling (Rodgers et al., 1983). From the predicted rate constant of 0.16 hour^{-1}, the half-life for evaporation can be estimated to be 4.3 hours. Volatilization, therefore, appears to be the primary removal process for naphthalene from water.

The removal of naphthalene from water by sedimentation was studied by Lee et al. (1978) in a controlled ecosystem enclosure, where 11% of the total naphthalene originally present in the water was recovered in the bottom sediment. Herbes et al. (1980) also estimated that ~15% of total amount of naphthalene added to a shallow, rapidly flowing stream is lost through sediment sorption.

Lee et al. (1978), Herbes et al. (1980) and Rodgers et al. (1983) predicted that microbial degradation and volatilization are the main processes for the removal of naphthalene from water. Removal through sediment sorption, however, may become important in bodies of water where the concentration of suspended solid is relatively high and water movement is slow, as in lakes and reservoirs (Herbes et al., 1980). The overall persistence of naphthalene in river water was experimentally determined by monitoring the level of naphthalene at two different points downstream from the source of pollution (Zoeteman et al., 1980); the estimated overall half-life (half-life from all processes) was 2.3 days.

Using correlation equations, Kenaga (1980) predicted the BCF for naphthalene in aquatic organisms to range from 80-88. Matsuo (1981) estimated a BCF value of 65 for naphthalene. BCFs in the range of 20-80 were determined for naphthalene in the dry tissue of coho salmon, O. Kisutch (Roubal et al., 1978). The average BCF value for naphthalene in the oyster, C. Virginica exposed to naphthalene for 15 days was 331 (Lee, 1977b). These studies indicate that naphthalene will not significantly bioaccumulate in edible parts of aquatic organisms.

2.3. SOIL

The fate of naphthalene in soil is not as well studied as its fate in water, but in cases where experimental data on its fate in soil are unavailable, qualitative predictions can be made from its known behavior in water (see Section 2.2.). Thus, microbial transformation of naphthalene in soil is likely to be a significant process. From their infiltration study of river water to groundwater, Schwarzenbach et al. (1983) concluded that biological transformation or mineralization by aerobic respiration was primarily responsible for the observed attenuation of naphthalene concentration in groundwater. They also observed that the biodegradation process occurred primarily within the first few meters of infiltration and that biological processes were quite efficient even at temperatures as low as 5°C. Ehrlich et al. (1982) found no evidence for anaerobic biodegradation of naphthalene under either field or laboratory conditions, yet the decrease in the concentration of naphthalene as a result of infiltration through soil could be attributable to biodegradation. This would indicate that aerobic degradation of naphthalene near the surface of the soil was responsible for the observed decrease in naphthalene concentration.

From their field data of a groundwater recharge project, Rittman et al. (1980) concluded that biodegradation was primarily responsible for the removal of naphthalene during soil infiltration. Studies indicate that naphthalene is only weakly sorbed in most soil, and the observed attenuation of naphthalene concentration in water as a result of percolation through soil cannot be attributed to sorption (Goerlitz et al., 1985; Schwarzenbach et al., 1983; Ehrlich et al., 1982). The third process that may be responsible for the loss of naphthalene from soil is volatilization (Bouwer et al., 1984; Jury et al., 1984). Jury et al. (1984) estimated the volatilization half-lives for naphthalene from different depths of a soil containing

1.25% organic carbon. The estimated half-lives were 1.1 day from a soil depth of 1 cm and 14.0 days from a soil depth of 10 cm. These results indicate that volatilization may be significant only from soil surfaces. Since the removal of naphthalene occurs in the top meter of soil, volatilization from the top layer may be an important process. In cases of near saturation of soil, however, as in the case of flooding, the reduction of naphthalene concentration through volatilization is not likely to be as important (Bouwer et al., 1984). The overall half-life (from all removal processes) of naphthalene in a polluted (solid waste) site was estimated to be 3.6 months (Zoeteman et al., 1981). Therefore, contamination of groundwater by naphthalene is likely from waste disposal sites.

2.4. SUMMARY

The most significant fate process for naphthalene in the atmosphere is likely to be its reaction with HO radical. From the measured rate constant in the range of 1.6×10^{-11} to 2.42×10^{-11} cm^3 $molecule^{-1}$ sec^{-1} (Lorenz and Zellner, 1983; Atkinson et al., 1984a) at 25°C and the average atmospheric HO• concentration of 10^6 molecules cm^{-3} (Cupitt, 1980), the half-life of naphthalene that is due to its reaction with HO radical has been estimated to be 8-12 hours. In photochemical smog systems, NO_3 radical formed at an average concentration of 2×10^9 molecule cm^{-3} (Atkinson et al., 1984b) can react with naphthalene having a rate constant of 6.4×10^{-13} cm^3 $molecule^{-1}$ sec^{-1} (Atkinson et al., 1984b); the estimated half-life for this reaction is 15 hours. Although no experimental data is available, naphthalene's physical properties suggest that significant removal of atmospheric naphthalene through physical processes (wet and dry deposition, etc.) are unlikely.

The two most important processes likely to remove naphthalene from water are volatilization and biodegradation (Lee et al., 1978; Herbes et al., 1980; Rodgers et al., 1983). The volatilization half-life of naphthalene at a current velocity of 0.1 m/sec and a wind velocity of 2 m/sec was estimated to be 60 hours, while the half-life was estimated to be 5 hours at a current velocity of 1 m/sec and a wind velocity of 3 m/sec (Southworth, 1979). Herbes et al. (1980) predicted the contributions of different processes in the removal of naphthalene from water in a shallow, rapidly flowing stream as follows: photolysis, <1%; microbial degradation, 4.4%; sediment sorption, 15.5%; and volatilization, 80%. The overall half-life of naphthalene in river water was experimentally determined to be 2.3 days (Zoeteman et al., 1980). The BCF of naphthalene in aquatic organisms, determined through correlation equations and by experimental methods, indicate values in the range of 20-90 (Kenaga, 1980; Roubal et al., 1978; Lee, 1977b; Hansen et al., 1978). When exposed to naphthalene-contaminated water for 16 days, the BCF value in the bile of trout, Salmo gairdneri, was reported to be 19,200 (Lech and Bend, 1980). All the studies indicate that naphthalene will not significantly bioaccumulate in edible portions of aquatic organisms.

Biodegradation and volatilization from soil surfaces are the two important processes for the removal of naphthalene from soil (Schwarzenbach et al., 1983; Bouwer et al., 1984; Jury et al., 1984). The estimated volatilization half-lives for naphthalene from a soil containing 1.25% organic carbon were as follows: 1.1 day from soil 1 cm deep and 14 days from soil 10 cm deep (Jury et al., 1984). The overall half-life of naphthalene in soil from a waste disposal site was estimated to be 3.6 months (Zoeteman et al., 1981). Therefore, contamination of groundwater by naphthalene is likely to occur from waste disposal sites.

3. EXPOSURE

3.1. AIR

Naphthalene has been detected in ambient air in the United States and other parts of the world. It has been reported in a rural (TerVuren) area of Belgium (Termonia and Alaerts, 1985), in three urban areas (Pretoria, Johannesburg, Durban) of South Africa (Louw et al., 1977) and in six industrial cities (Baku, Kemerovo, Leningrad, Murmansk, Tashkent, Tbidisi) in the Soviet Union (Ioffe et al., 1977, 1979). Thrane and Mikalsen (1981) determined the levels of naphthalene in rural (Birkenes), suburban (Lillestrom) and urban (Oslo) areas of Norway. The average concentration of naphthalene was <4 ng/m³ in the rural samples, ~27 ng/m³ in the suburban samples, and in the range of 66-670 ng/m³ in urban samples. The concentration of naphthalene in the atmosphere of Paris, France, was reported to range from 3.8-11.2 μg/m³ (Raymond and Guiochon, 1974).

Krstulovic et al. (1977) reported the atmospheric level of naphthalene in rural Rhode Island (Narragansett Bay) as 0.05 ng/m³. The measured levels in suburban (Kingston) and urban (Providence) areas of Rhode Island were 0.06 and 0.35 ng/m³, respectively. Jarke et al. (1981) measured the frequency of occurrence of naphthalene in Chicago area homes and found that it was twice as high as outdoor air. The levels of atmospheric naphthalene in several urban/suburban and source-dominated areas in the United States were reported by Brodzinsky and Singh (1982) to be 180 and 400 ppt (940 and 2100 ng/m³), respectively.

Naphthalene concentrations inside Allegheny Tunnel, Pennsylvania, where the level of several polycyclic aromatic hydrocarbons including naphthalene are expected to be higher than ambient levels, was reported to vary between 3.5 and 10.1 μg/m³ (Hampton et al., 1983). The levels of naphthalene in

indoor and outdoor air at an oil shale wastewater facility in Laramie, WY, were reported to be 7 and 0.1 μg/m³, respectively (Hawthorne and Sievers, 1984). Hawthorne and Sievers (1984) also measured the levels of naphthalene in the atmosphere of Boulder, CO, and a rural area of the oil shale region and reported concentrations of 100 and <50 ng/m³, respectively. Bjorseth et al. (1978) determined that the level of naphthalene near a Norwegian aluminum reduction plant (Soderberg) was as high as 311.3 μg/m³.

Based on 940 ng/m³ as median urban/suburban concentraion and 2100 ng/m³ as the median source area concentration for naphthalene in United States atmosphere (Brodzinsky and Singh, 1982) and an inhalation rate of 20 m³/day by an individual, the daily exposures to atmospheric naphthalene have been estimated to be 18.8 and 42 μg, respectively.

3.2. WATER

Concentrations of naphthalene in a Norwegian sewage treatment plant effluent were reported to be 88 ng/ℓ during a fall dry period, 303 ng/ℓ during a dry period in spring and 1504 ng/ℓ after a rainfall in the summer (Kveseth et al., 1982). The concentrations of naphthalene in the influent and effluent water in Philadelphia's Northeast sewage treatment plant were reported to be 20 and 4 μg/ℓ, respectively (Hites, 1979). The concentration of naphthalene in tire plant effluent was reported to be 100 μg/ℓ (Jungclaus et al., 1976). The concentration of naphthalene in wastewater of a specialty chemical plant was reported to be in the range of 1-4 mg/ℓ (Jungclaus et al., 1978). Naphthalene levels in the raw sewage of a large municipal treatment plant in Chicago were as high as 42.3 μg/ℓ, but were reduced to a level of <0.5 μg/ℓ in the final effluent

(Lue-Hing et al., 1981). Keith (1974) also reported the detection of naphthalene in wastewater from a petroleum company. Callahan et al. (1979) measured the levels of naphthalene in wastewater from suspected pollution sources and in influents in wastewater treatment plants in two Midwestern cities in the United States; the frequency of occurrence of naphthalene in source samples was 14 and 23%, with an average concentration of 8 and 23 µg/ℓ, and the corresponding values for the treatment plant influent samples were slightly higher. Cole et al. (1984) reported the detection of naphthalene in runoff water samples from several urban areas with a frequency of 11% and an average concentration range of 0.8-2.3 µg/ℓ.

In the surface water of an unidentified river near a specialty chemical plant, Jungclaus et al. (1978) reported naphthalene in the concentration range of 6-10 µg/ℓ. In Delaware River water near Philadelphia a maximum concentration of 0.7-0.9 µg/ℓ naphthalene was reported (Sheldon and Hites, 1978, 1979). Naphthalene was also detected in water from the Charles River in Boston (Hites and Biemann, 1972). Naphthalene was also detected in Mississippi River water (Goodley and Gordon, 1976; Overton et al., 1980). Sauer (1981) reported up to 5 µg/ℓ of naphthalene in surface water from the Gulf of Mexico. Naphthalene was also detected in water from Narragansett Bay (Wakeham et al., 1983). Grob and Grob (1974) detected naphthalene up to a concentration of 0.052 µg/ℓ in water from Lake Zurich, Switzerland.

Naphthalene contamination in groundwater near waste sites has also been reported. Bedient et al. (1984) reported concentrations up to 926.4 µg/ℓ in well water near an abandoned creosote facility in Conroe, TX. Naphthalene concentrations up to 1800 µg/ℓ were reported in groundwater near an underground coal gasification site in northeastern Wyoming (Stuermer

et al., 1982). Reinhard et al. (1984) detected a maximum level of 110 µg/ℓ naphthalene in leachates from sanitary landfill sites. Concentrations of naphthalene as high as 155 µg/ℓ were reported in groundwater located 20 m from a fuel spillage site (Tester and Harker, 1981). Staples et al. (1985) used U.S. EPA's STORET data points accumulated since the 1980s to determine the concentration of various pollutants in effluent and ambient water samples. Of the 1206 effluent samples analyzed, only 1.6% of the samples showed detectable levels of naphthalene. The median concentration of naphthalene in all effluent samples was <10 µg/ℓ. Similarly, of the 630 ambient water samples, only 7% contained naphthalene, and the median concentration for all samples was <10 µg/ℓ.

Callahan et al. (1979) monitored drinking water samples from two Midwestern cities in the United States. No naphthalene was detected in any of these waters at a detection limit of 10 µg/ℓ. On the other hand, a naphthalene concentration of 1 µg/ℓ was detected in District of Columbia drinking water (Scheiman et al., 1974). In Ottawa, Canada, tap water, Benoit et al. (1979) detected naphthalene in the concentration range of 4.8-6.8 µg/ℓ. In tap water in Kitakyushu, Japan, Shinohara et al. (1981) reported the detection of 2.2 µg/ℓ of naphthalene. The concentrations of naphthalene in Nordic tap water were reproted to vary between 1.2 and 8.8 ng/ℓ (Kveseth et al., 1982). Grob and Grob (1974) reported a naphthalene concentration of 8 ng/ℓ in tap water from Zurich, Switzerland.

Human exposure to naphthalene from drinking water in the United States cannot be estimated since the median or average concentration of this chemical in drinking water is not available.

3.3. FOOD

Naphthalene has been detected in several food items consumed by humans. The concentration of naphthalene in mussels, Mytilus edulis and M. californianus collected from the East, West and Gulf Coasts of the United States contained 2.8-96 µg/kg (dry wt.) of naphthalene (Galloway et al., 1983). Knutzen and Sortland (1982) detected trace to 516 µg/kg (dry wt.) of combined naphthalene and methyl naphthalene in the common mussel, Mytilus edulis, collected from the Norwegian coast; unfortunately, their method could not separate naphthalene from methyl naphthalene. The concentration of naphthalene in snails, Cipargopaludina chinensis, collected from the marshes of the Royal Botanical Gardens in Hamilton, Ontario, was reported to be <0.01 µg/kg (dry wt.) (Kalas et al., 1980). Naphthalene at a maximum concentration of 7.88 µg/kg (dry wt.) was detected in traditionally preserved Nigerian freshwater fish species (Afolabi et al., 1983). Naphthalene at a concentration of 22 µg/kg (dry wt.) was reported to be present in smoked Japanese horse mackeral (Fazio and Howard, 1983). Pellizzari et al. (1982) detected naphthalene in 6/12 samples of milk collected from lactating mothers from areas of New Jersey, Pennsylvania and Louisiana. Human exposure to naphthalene from ingestion of foods cannot be estimated unless the composite levels of this compound in foods from market basket surveys become available.

3.4. SUMMARY

Naphthalene has been detected in ambient air in the United States and other parts of the world. The median concentrations of naphthalene in U.S. urban/suburban and source-dominated atmospheres were 940 and 2100 ng/m³, respectively (Brodzinsky and Singh, 1982). Based on these values and a human air inhalation rate of 20 m³/day, the daily exposures to atmospheric naphthalene have been estimated to be 18.8 and 42 µg, respectively.

Naphthalene has been detected in wastewater, urban runoff water, surface waters and groundwater from contaminated sites. For example, naphthalene concentrations in the wastewater of a speciality chemical plant were reported to range from 1-4 mg/ℓ (Jungclaus et al., 1978). Naphthalene at a concentration of 1.8 mg/ℓ was reported in groundwater near an underground coal gasification site in northeastern Wyoming (Stuermer et al., 1982). Naphthalene has been detected in drinking water samples in the United States and elsewhere in the world. The concentration of naphthalene in a District of Columbia drinking water was reported to be 1 µg/ℓ (Scheiman et al., 1974). In Ottawa, Canada, tap water, Benoit et al. (1979) detected naphthalene in the concentration range of 4.8-6.8 ng/ℓ. Grob and Grob (1974) reported a naphthalene concentration of 8 ng/ℓ in tap water from Zurich, Switzerland. The human exposure to naphthalene from drinking water in the United States cannot be estimated unless additional monitoring data become available.

Several food items have been reported to contain naphthalene. The concentration of naphthalene in mussels, Mytilus edulis and M. californian, may be as high as 96 µg/kg (dry wt.) (Galloway et al., 1983). A naphthalene concentration of 22 µg/kg (dry wt.) was reported in smoked Japanese horse mackeral (Fazio and Howard, 1983). Pellizzari et al. (1982) detected naphthalene in 6/12 samples of mothers' milk collected from three states in the United States. Human exposure to naphthalene from ingestion of foods cannot be estimated unless composite levels of naphthalene in foods from market basket surveys are available.

4. PHARMACOKINETICS

4.1. ABSORPTION

Quantitative data regarding the gastrointestinal, pulmonary or dermal absorption of naphthalene could not be located in the available literature as cited in the Appendix. Reports from the older literature and from secondary sources indicate qualitatively that pulmonary and gastrointestinal absorption occurs. Naphthalene can be sufficiently absorbed when ingested as a solid to result in toxicity in man (Chusid and Fried, 1955; Zuelzer and Apt, 1949; Nash, 1903; Gross et al., 1958; Haggerty, 1956). Summer et al. (1979) administered single gavage doses of naphthalene of 0, 30, 75 or 200 mg/kg to adult male SPF Wistar rats and observed a dose-related increase in the 24-hour urinary excretion of thioethers, representing 26-39% of the administered dose. These data suggest that the rate of absorption of a single dose of naphthalene to rats remains fairly constant up to 200 mg/kg. The oral toxicity of naphthalene and a metabolite of naphthalene (1,4-naphthoquinone) were markedly increased when the compounds were dissolved in oil before administration (Solomon, 1957; Talakin, 1966). However, recent studies (Doull, 1980; Withey et al., 1983; Bull et al., 1986) have shown that corn oil may be a confounding factor in the interpretation of these earlier findings. The results from the more recent studies have indicated that the use of corn as a vehicle for nonpolar compounds may alter the absorption, distribution, metabolism and/or elimination of the compound. In addition, saturated hydrocarbons (corn oil, etc.) may alter the nutritional status of the animal and induce the formation of fatty livers (Doull, 1980). Studies by Sanborn and Malins (1977) have suggested that naphthalene may be absorbed to a greater extent when ingested in water than in food. The authors attributed the decrease in food absorption to the binding of

naphthalene to proteins in food. Humans absorb naphthalene most readily by the inhalation route (Sandmeyer, 1981). Absorption of naphthalene vapors from clothing or blankets resulted in toxicity and death to newborn infants (Valaes et al., 1963). Mackell et al. (1951) found metabolites of naphthalene in the urine of an 18-month-old infant exhibiting toxic signs of naphthalene exposure.

4.2. DISTRIBUTION

Naphthalene was identified in all tissues of mallards orally given naphthalene in oil over a 2-week period. Its relative distribution was as follows: skin > liver > brain = blood > muscle > heart (Lawler et al., 1978). Intraperitoneal administration of radioactively labeled naphthalene in mice resulted in covalent bonding of radiolabel to tissue macromolecules (Warren et al., 1982). Highest levels of binding occurred in the lung, liver and kidney, with levels reaching a maximum 2-4 hours after treatment.

The distribution of ^{14}C-naphthalene in the tissues of laying pullets, swine and dairy cattle was evaluated after acute and subchronic oral exposure to the compound (Eisele, 1985). Doses for acute single exposures were 0.443, 2.46 and 30.69 mg, and doses for subchronic 31-day exposures were 0.036, 0.112 and 5.115 mg/day, respectively, for pullets, swine and dairy cows. In pullets, major sites of deposition of radioactivity were the kidneys, fat, lungs and liver, following acute exposures. In the subchronic study, the liver showed twice the activity of the fat. Regardless of the time of administration, the dark meat retained more radioactivity than the white. The yolk was shown to be the preferred site of deposition within the egg. The major site of deposition in swine following acute exposure to naphthalene was the fat, followed by the liver. After chronic exposure, however, the major sites of deposition were the lung, liver and heart with

little retention of radioactivity in the fat. Tissue distribution of radioactivity in dairy cows was found to be comparable in both acute and chronic exposures. The liver was the major site of deposition and radioactivity was detected in the milk equally distributed between the fat and the nonfat portion. Differences in the distribution pattern resulting from acute vs. subacute exposures may be due to the saturation of metabolic pathways by the larger acute doses. As a result the ratio of parent to metabolites may be different; however, further characterization of the label is necessary to substantiate this.

4.3. METABOLISM

Based on in vitro studies with liver microsomal and supernatant preparations from phenobarbital-induced rats, Jerina et al. (1968, 1970) suggested that naphthalene in mammals is first metabolized by the liver to the epoxide, naphthalene 1,2-oxide. This epoxide can then undergo conversion to the dihydrodiol, 1,2-dihydroxy-1,2-dihydronaphthalene, or can be conjugated with glutathione, or can convert spontaneously to 1- or 2-naphthol (Boyd et al., 1972). Chen and Dorough (1979) found that glutathione conjugates and mercapturic acid-related products were the major metabolites formed in the rat. In vitro, the metabolism of ^{14}C-naphthalene produced 50% glutathione conjugates in the incubation mixture, but the proportion of glutathione conjugates depended on the amount of glutathione added to the substrate mixture. Inhibition of glucuronidation and sulfation causes a dramatic increase in the accumulation of reactive metabolites in isolated rat hepatocytes exposed to naphthalene, suggesting that conjugation plays an important part in the detoxification of naphthalene (Schwartz et al., 1980; Hesse et al., 1982; Hesse and Merger, 1979; Oesch and Daly, 1972). Chen and Dorough (1979) administered a single 100 mg/kg intraperitoneal dose of ^{14}C-naphthalene to

mature female Sprague-Dawley rats and collected urine separately from feces for 72 hours. Seventy-two hour urine and feces collections contained 60 and 14%, respectively, of the administered dose of radioactivity. The urine was extracted with ether to separate polar and nonpolar metabolites. The ether extract contained radioactivity equivalent to 6% of the administered dose and consisted principally of 1-naphthol and 1,2-dihydro-1,2-dihydroxynaphthalene at 60 and 28% of the ether extractable radioactivity, respectively. Water soluble metabolites consisted of 1-naphthol, 1,2-dihydro-1,2-dihydroxy-1-naphthyl sulfate, N-acetyl-S-(1,2-dihydro-2-hydroxy)-1-naphthyl cysteine (designated a "premercapturic" acid), and 1,2-dihydro-2-hydroxy-1-naphthyl glucuronide at 5.0, 8.0, 65.0 and 16.8% of the radioactivity in the urine remaining after ether extraction. Rozman et al. (1982) and Summer et al. (1979) reported that conjugation of naphthalene and its metabolites with glutathione does not appear to play a major role in the metabolism of naphthalene in primates.

Summer et al. (1979) administered single gavage doses of naphthalene of 0, 30, 75 or 200 mg/kg to two male and two female yearling chimpanzees and five adult male SPF Wistar rats and determined urinary excretion of thioethers (mercapturic acids) as an indication of the extent of glutathione conjugations. Excretion of thioethers by rats increased in a dose-related manner; at 0, 30, 75 and 200 mg naphthalene/kg, urinary output of thioethers was measured at 94.4, 185.6, 279.6 and 502.0 µmol/24 hour/kg, respectively. The increase in urinary thioethers in treated rats represented 26-39% of the dose of naphthalene. Treatment of chimpanzees with naphthalene did not result in increased urinary output of thioethers (measured at 0 and 200 mg/kg). The urinary output of nontreated chimpanzees (18.0 µmol/24 hour/kg) is substantially less than that of nontreated rats (94.4 µmol/

24 hour/kg). Urinary output of thioethers by nontreated humans was determined to be 22.8 μmol/24 hour/kg, much closer to that of chimpanzees than of rats. The authors suggested that these differences within species in urinary output of thioethers following treatment with naphthalene reflect species differences in substrate-specific activities of glutathione-S-transferases. The chimpanzee was recommended as a more appropriate model than the rat for studying human metabolism of xenobiotics that are conjugated with glutathione more readily by rats than by humans. However, biliary excretion of glutathione conjugates of naphthalene, a logical route of excretion for metabolites of this size, was not investigated in this experiment.

Several other metabolites of naphthalene have been found in lung and hepatic cells and microsomal preparations (U.S. EPA, 1980a; Holtzman et al., 1967; Buckpitt, 1982, 1983; Buckpitt et al., 1985). Mackell et al. (1951) identified these metabolites of naphthalene in human urine: 1-naphthol, 2-naphthol, 1,2-naphthoquinone, 1,4-naphthoquinone.

Naphthalene metabolites undergo further conversions in the eye. The 1,2-naphthoquinone metabolite binds irreversibly to lens protein and amino acids, and reacts with glutathione (Van Heyningen and Pirie, 1966, 1967; Gehring, 1971; Rees and Pirie, 1967). Van Heyningen (1979) later suggested that naphthalene-induced cataract formation in rats and rabbits was caused by the formation of 1,2-dihydroxynaphthalene in the eye, which autoxidizes to 1,2-naphthoquinone.

Several investigators have also observed that reactive metabolites from the cytochrome P-450-mediated metabolism of naphthalene deplete pulmonary glutathione and become covalently bound to tissue macromolecules, resulting

in damage to the bronchiolar epithelium (Buckpitt and Warren, 1983; Buckpitt, 1982, 1983; Tong et al., 1981, 1982). These same studies suggested that some of the reactive metabolites which deplete glutathione in extrahepatic tissues and bind covalently to the macromolecules, orginate in the liver.

4.4. EXCRETION

The literature is replete with reports of metabolism studies in which urinary metabolites are identified and metabolic pathways are proposed, but limited quantitative data were located regarding the excretion of naphthalene and its metabolites from the body. Chen and Dorough (1979) administered a single 100 mg/kg intraperitoneal dose of ^{14}C-naphthalene to adult female Sprague-Dawley rats and collected urine and feces for 72 hours. By 24 hours, urinary radioactivity accounted for 24% of the administered dose. Total recovery of radioactivity at the end of the 72-hour collection period was 74% of the administered dose; 60% in the urine and 14% in the feces. Further quantitative studies including studies on pulmonary elimination are needed to fully characterize the excretion of naphthalene and its metabolites from the body.

4.5. SUMMARY

Absorption of naphthalene in man and animals has been demonstrated by oral and inhalation exposure (Chusid and Fried, 1955; Zuelzer and Apt, 1949; Nash, 1903; Gross et al., 1958; Haggerty, 1956; Valaes et al., 1963; Sandmeyer, 1981). Its oral absorption may be enhanced by solution in oil or ingestion in water rather than in food. Naphthalene has been shown to distribute in a wide variety of tissues of several species following absorption (Lawler et al., 1978; Eisele, 1985). Highest levels appear in the liver, kidneys and lungs of most species tested. In treated swine, levels are high

in fat after a single treatment, but higher in liver and lower in fat after treatment for 31 days (Eisele, 1985). While naphthalene itself has not been identified in the urine after absorption, its metabolites have been identified in humans, rats and mice (Mackell et al., 1951; Horning et al., 1980; Stillwell et al., 1978, 1979, 1980). Naphthalene is first converted to naphthalene, 1,2-oxide in the liver by a cytochrome P-450-dependent monooxygenase (Jerina et al., 1968, 1970). The reactive epoxide is converted to other oxidation products and is detoxified by conjugation with glutathione (Boyd et al., 1972). In the rat, glutathione conjugation is a major metabolic pathway (Chen and Dorough, 1979; Summer et al., 1979), but further studies are necessary to access the significance of this pathway in primates. Naphthalene dihydrodiol released from the liver can be converted in the eye to 1,2-napthoquinone, causing toxic reactions such as cataracts (Van Heyningen and Pirie, 1966, 1967; Rees and Pirie, 1967; Van Heyningen, 1979). Reactive metabolites from the cytochrome P-450-mediated metabolism of naphthalene in the liver have also been shown to deplete pulmonary glutathione and become covalently bound to tissue macromolecules, resulting in damage to the bronchiolar epithelium (Buckpitt and Warren, 1983; Buckpitt, 1982, 1983; Tong et al., 1981, 1982). Rats treated with intraperitoneal ^{14}C-naphthalene excreted 24% of the dose of radioactivity in the urine by 24 hours and 60% in the urine by 72 hours. By 72 hours, 14% of the dose of radioactivity had been recovered from the feces.

5. EFFECTS

5.1. CARCINOGENICITY

Malignant tumors were reported in 6/15 workers at a coal tar/naphthalene production facility where they had been exposed to vapors of naphthalene and coal tar for up to 32 years (Wolf, 1976). All of the workers were smokers; four developed laryngeal carcinomas and the other two developed tumors of the pylorus and cecum.

Knake (1956) administered 500 mg/kg coal tar naphthalene in sesame oil subcutaneously to 40 white rats every 2 weeks for seven treatments and observed the animals for 18 months. In the naphthalene-treated group, 34/40 rats survived the treatment and 5 developed invasive or metastatic lymphosarcomas before death. In the group injected with sesame oil (3.3 mg/kg) alone, 32/40 animals survived and 1 developed a lymphosarcoma. The incidence of malignancies in the untreated control group was ~2%, similar to the group treated with sesame oil alone. The injection sites of the naphthalene and sesame oil-treated groups were painted with carbolfuchsin, a known experimental carcinogen, before each injection. It was also reported that the naphthalene contained impurities equivalent to 10% methyl naphthalene.

In another study, Knake (1956) painted groups of inbred black mice with either benzene (n=21) or a 0.5% solution of coal tar naphthalene in benzene (n=25), 5 days/week for life. The naphthalene-treated group showed higher incidences (4/25) of lymphatic leukemia than the benzene treated group (0/21) or the untreated historic controls (5/1227).

Schmahl (1955) investigated the carcinogenic potential of naphthalene administered orally and by intraperitoneal and subcutaneous injection in rats strain BDI and BDII. In the oral study, a group of 28 rats was given naphthalene in daily doses (6 days/week) between 10 and 20 mg/day up to a

total dose of 10 g/rat over a 700-day period. In the injection studies, a group of 10 rats received either a single intraperitoneal or subcutaneous dose of 20 mg/naphthalene/rat weekly for 40 weeks (total dose of ~820 mg/rat). The observation period for all experiments was up to 1000 days. All animals were necropsied and histopathology was performed on any "unusual" looking organs. No carcinogenic responses were observed in any of the groups.

U.S. EPA (1980a) briefly summarized other experiments that were insufficiently reported or otherwise seriously flawed and which showed no significant increase in naphthalene-induced tumor formation (Boyland et al., 1964; Kennaway, 1930; Kennaway and Hiegel, 1930; Bogdat'eva and Bid, 1955; Schmeltz et al., 1978).

Tsuda et al. (1980) administered a single gavage dose of naphthalene in corn oil of 100 mg/kg to a group of 10 young adult F344 rats (sex not specified) at 12 hours after partial hepatectomy. A vehicle control group was included. At 2 weeks after surgery, 2-acetylaminofluorene was added to the diet at 200 ppm to inhibit proliferation of "nonresistant" hepatocytes. After 1 week of dietary 2-acetylaminofluorene, a single 2.0 mL/kg dose of carbon tetrachloride was given to necrotize "nonresistant" hepatocytes and permit proliferation of "resistant" hepatocytes. Feeding of 2-acetylaminofluorene continued for 1 week, followed by a basal diet for 1 week. The rats were then sacrificed and livers were sectioned and histochemically examined for the number and size of γ-GT positive foci. These foci contain cells that are "resistant" to the necrotizing effects of carbon tetrachloride and to the proliferation-inhibiting effects of 2-acetylaminofluorene and are considered to represent preneoplastic transformations. An increase in the number or size of γ-GT containing foci in chemically

treated rats is, therefore, considered to be evidence suggesting a carcinogenic role for the test chemical. Neither the number nor the size of γ-GT foci appeared to be increased in naphthalene-treated rats compared with vehicle controls.

Naphthalene is currently being evaluated for carcinogenicity in mice by inhalation at doses of 10 or 30 ppm by the National Toxicology Program. Final results are not available, and chronic histopathology is currently in progress (NTP, 1985).

5.2. MUTAGENICITY

Results of mutagenicity testing are summarized in Table 5-1. Naphthalene has been found to be consistently nonmutagenic in several microsomal/bacterial assay systems (McCann et al., 1975; Seixas et al., 1982; NTP, 1982; Anderson and Styles, 1978; Hermann, 1981; Kaden et al., 1979; Mamber et al., 1983). Sina et al. (1983) reported naphthalene to show no genotoxic activity in cultured rat hepatocytes when evaluated for the induction of DNA strand breaks.

Naphthalene has been tested for cell transformation activity in systems using rat and mouse embryo cells pretreated with leukemia virus (Freeman et al., 1973; Rhim et al., 1974) and murine mammary gland organ cultures (Tonelli et al., 1979). No transforming activity was observed.

5.3. TERATOGENICITY

Results of teratogenicity reports are summarized in Table 5-2. A Russian study (Matorova and Chetverikova, 1981) evaluated the embryotoxic effect of naphthalene administered intragastrically to pregnant female rats in doses of 70, 0.15 and 0.075 mg/kg for 19 days. The rats were sacrificed on day 19 of gestation and the fetuses removed for evaluation. No visible developmental defects were found in any of the fetuses and no visible or microscopic anomalies were found in the group administered a 0.075 mg/kg

TABLE 5-1

Mutagenicity Testing of Naphthalene

Assay	Indicator/ Organism	Compound and/or Purity	Application	Concentration or Dose	Activating System	Response	Reference
Reverse mutation	Salmonella typhimurium TA98, TA100, TA1535, TA1537	commercial	plate incorporation test	0, 10, 100, 500 and 1000 µg	±S-9	-	McCann et al., 1975
Reverse mutation	S. typhimurium	NR	pre-incubation	up to 1.6 mM	±S-9	-	Seixas et al., 1982
Reverse mutation	S. typhimurium TA98, TA100, TA1535, TA1537	99.8%	pre-incubation	0.3, 1.0, 3.3, 10, 33 and 100 µg	±S-9	-	Mortelmans et al., 1986
Reverse mutation	S. typhimurium TA98, TA100, TA1535, TA1538	NR	plate incorporation	4, 20, 100, 500 and 2500 µg/plate	±S-9	-	Anderson and Styles, 1978
Reverse mutation	S. typhimurium TA98	commercial	plate incorporation	NR	±S-9	-	Hermann, 1981
Reverse mutation	S. typhimurium TA97, TA98, TA100	NR	plate incorporation	5, 10, 50, 250 µg	±S-9	-	Sakai et al., 1985
Forward mutation	S. typhimurium TM677	NR	pre-incubation	up to 1.6 mM	±S-9	-	Seixas et al, 1982
Forward mutation	S. typhimurium TM677	commercial	plate incorporation	up to 2 mM	±S-9	-	Kaden et al., 1979
Rec assay	Escherichia coli WP2/WP67 Pol W311/P3478 Pol	NR	spot test	≤2000 µg/L	±S-9	-	Mamber et al, 1983
DNA damage	rat hepatocyte	NR	cell culture	0.03, 0.3 and 3 mM	NA	-	Sina et al., 1983
Transformation	rat embryo cells	NR	cell culture	0.05, 1.0, 5.0, 10, 50 and 100 µg/mL	none	-	Freeman et al., 1973
Transformation	NIH Swiss mouse embryo cells	NR	cell culture	0.1, 0.5, 1.0 and 5.0 µg/mL	none	-	Rhim et al., 1974
Transformation	murine mammary gland	commercial	organ culture	0, 0.001, 0.01, 0.1 and 1.0 µg/mL gland	none	-	Tonelli et al., 1979

NR = Not reported; NA = not applicable

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TABLE 5-2

Teratogenicity Testing of Naphthalene

Route	Species/ Strain	No. of Dams at Start	Vehicle	Daily Dose (mg/kg)	Treatment Days	Observation Days	Maternal Response	Fetal Response	Reference
Intragastric	white mongrel rats	7-8	oil	0.075, 0.15 and 70	1-19 of gestation	day 19 of gestation	NR	0.075 mg/kg NOAEL; significant embryonic mortality, preimplantation mortality and a significant number of feluses with subcutaneous hematomas at 0.15 and 70 mg/kg; no visible developmental defects in any group	Matorova and Chetverikova, 1981
Intragastric	CD-1 mice	50	corn oil	300	7 of gestation for 8 consecutive days	through parturition	increased mortality, reduced body weight gain	Reduced number of live young at birth	Plasterer et al., 1985
Intraperitoneal	adult female Sprague-Dawley rats	NR	NR	395	1-15 of gestation	1 day before parturition	NR	Retarded cranial ossification and heart development	Harris et al., 1979
Intraperitoneal	adult female Sprague-Dawley rats	10-15	corn oil	395	1-15 of gestation	day 21 of gestation	no effect on body weight gain on organ weights	No fetal toxicity (fetal body weight or length, pre- or postimplantation survived); no grossly visible external or internal malformations	Hardin et al., 1981

NR = Not reported

dose of naphthalene. A significant number of fetuses from the 70 and 0.15 mg/kg group had subcutaneous hematomas on the spine and extremities. Embryonic mortality and preimplantation mortality was significantly higher in these groups than in the controls. When treated pregnant females were allowed to give birth naturally, the pregnancies lasted longer than in the control group (up to 27 days). At 0.15 and 70 mg/kg, rats were born with black tails that fell off 6-8 hours later. Again, higher mortality and increased hematomas were observed in the treated groups.

Plasterer et al. (1985) administered naphthalene at 300 mg/kg/day by gavage to groups of 50 mated female CD-1 mice. Treatment began on gestation day 7 and continued for 8 consecutive days. Vehicle (corn oil) treated controls were maintained. Treatment was associated with maternal toxicity (increased mortality and reduced weight gain) and fetotoxicity manifested as a reduced number of live young at birth that the authors attributed to early fetal resorptions. The young were not examined for terata.

Harris et al. (1979) reported the effects on fetal development after intraperitoneal injection of 395 mg/kg naphthalene administered to adult female Sprague-Dawley rats on days 1-15 of gestation. Control animals received 1 mg/kg corn oil and control and treated litters were collected 1 day before parturition. When compared with controls, pups from naphthalene-dosed dams showed twice the incidence of retarded cranial ossification and heart development. A later publication from the same laboratory (Hardin et al., 1981), however, reported no evidence of fetal or maternal toxicity when 395 mg/kg of naphthalene was administered intraperitoneally to Sprague-Dawley rats on days 1-15 of gestation. It is not clear if these two reports refer to the same study and the reasons for the apparent discrepancy are unclear.

5.4. OTHER REPRODUCTIVE EFFECTS

Naphthalene or its metabolites can cross the human placenta in amounts sufficient to cause fetal toxicity (U.S. EPA, 1980a; Bergheim et al., 1973). Human fetal kidney, liver and adrenal glands, however, have been shown to possess the enzymic capabilities for the conversion of an epoxide of naphthalene to three of its normal metabolites (Juchau and Namkung, 1974). Hemolytic anemia has been observed in infants of mothers exposed to naphthalene during pregnancy (Zinkham and Childs, 1958; Anziulewicz et al., 1959). Infants and adults with congenital erythrocyte glucose 6-phosphate dehydrogenase deficiency are more susceptible to naphthalene-induced hemolytic anemia (Nyhan, 1961; Sandmeyer, 1981; Valaes et al., 1963).

5.5. CHRONIC AND SUBCHRONIC TOXICITY

In a subchronic oral toxicity study performed for the NTP (1980a), naphthalene in corn oil was administered by gavage to male and female F344 rats (10/sex/dose) at dose levels of 0, 25, 50, 100, 200 or 400 mg/kg/day, 5 days/week for 13 weeks. At 400 mg/kg, two males died during the first week and the treatment caused diarrhea, lethargy, hunched posture and roughened haircoats in rats of both sexes. A significant (i.e., >10%) decrease in body weight gain was observed among males and females at 200 and 400 mg/kg and in females at 100 mg/kg. Food consumption was not affected.

All the rats in the study were necropsied and comprehensive histopathological examinations were performed on rats from the 0 and 400 mg/kg groups. Histopathological examinations of the kidneys and thymus were performed on rats from the 200 mg/kg group (according to the histopathology tables; the 100 mg/kg group according to the text). The authors stated that lesions of the kidney in males and thymus in females of the 400 mg/kg group may have been compound-induced, and that no eye lesions were found. The incidences

of lesions of kidney and thymus were, however, very low. The renal lesions, which did not occur in females, were observed at incidences of 0/10 in controls, 2/10 in the 200 mg/kg group and 1/10 in the 400 mg/kg group. These renal lesions consisted of focal cortical lymphocytic infiltration or focal tubular regeneration in the two 200 mg/kg males and diffuse tubular degeneration in the one 400 mg/kg male. Lymphoid depletion of the thymus occurred in 2/10 females of the 400 mg/kg group and in none of the control or 200 mg/kg females and in none of the males of these groups. Hematological analyses revealed marginal decreases in hemoglobin and hematocrit in males and females of the 400 mg/kg group, and a moderate increase in the number of mature neutrophils and a decrease in the number of lymphocytes in males of the 400 mg/kg group, relative to controls. No hematological changes were observed at the lower dosages.

In a similar study, naphthalene was administered in corn oil by gavage at 0, 12.5, 25, 50, 100 or 200 mg/kg/day, 5 days/week, to B6C3F1 mice (10/sex/dose) for 13 weeks (NTP, 1980b). Seven mice (three males and two females of the 200 mg/kg group, one female of the 25 mg/kg group and one control male) died during the 2nd, 3rd and 4th weeks of the study from gavage trauma or accident. Transient signs of toxicity (lethargy, rough haircoats and decreased food consumption) occurred at weeks 3-5 in the 200 mg/kg groups. All treated groups of male mice gained somewhat more weight than did control males. Dose-related decreases in body weight gain were seen in females, but were not significant. All the mice were necropsied and comprehensive histopathological examinations were performed on the mice from the 0 and 200 mg/kg groups. No compound-related lesions were observed in any organs, including kidneys, thymus, eyes and lungs. Hematological analyses, performed on all groups, revealed no significant, compound-related changes.

Shopp et al. (1984) evaluated the subchronic oral toxicity of naphthalene administered by gavage to 6-week-old female (40-76) and male (76-112) CD-1 mice for 90 days at doses of 5.3, 53 and 133 mg/kg/day. No compound-related mortality or changes in body weights of either sex were observed. All tests were performed on randomly selected animals (~9/sex/dose) from each group; histopathological parameters were not evaluated. No significant changes in organ weight were observed in the males, but absolute and relative spleen weights were reduced in the female mice at the high dose, possibly related to subclinical hemolysis (Malek and Colman, 1985), as discussed when mice were dosed at 267 mg/kg/day for 14 days (Shopp et al., 1984). No compound-related effects were seen on serum enzyme and electrolyte levels or immunological parameters based on a number of screening tests. There was no evidence of naphthalene-induced hemolytic anemia or cataract formation, although CD-1 mice may not be an appropriate model for these effects (Shichi and Nebert, 1982). Lung damage was not observed upon pathological examination. A significant dose-related inhibition of aryl hydrocarbon hydroxylase activity was observed in both sexes, but the toxicological significance of this finding is unclear. No other changes in hepatic microsomal activity were seen.

Additional information regarding the response at a high dosage was available in CD-1 mice following the administration of 27, 53 or 267 mg/kg/day by gavage in a preliminary 14-day study (Shopp et al., 1984). Compound-related increases in mortality, decreases in body weight, decreases in absolute thymus weight in males and in relative and absolute spleen and lung weights in females, were observed at 267 mg/kg/day. A significant increase in serum bilirubin was observed in females and an increase in

eosinophils in males. The increase in serum bilirubin in females may be an indication of hemolysis and the decreased spleen weight an indication of release of stored erythrocytes.

Schmahl (1955) administered naphthalene in the feed to BDI and BDII rats at a dose of 10-20 mg/day, 6 days/week, for 700 days; total dosage 10 g/rat. The rats were observed until they died spontaneously. Comprehensive gross and limited histopathological examination was performed. No compound-related effects on mortality were noted and lifespan of the animals was $\geq$800 days. No compound-related histopathology was reported, no eye damage occurred and no other signs of toxicity were reported.

5.6. OTHER RELEVANT INFORMATION

Van Heyningen and Pirie (1976) concentrated on ocular effects when they intubated adult albino and pigmented rabbits with 1 g/kg/day of naphthalene for up to 28 days. Eyes were examined daily and severe damage to retina and lens was reported. The authors observed lens changes developing after the first dose and retinal changes developing after the second dose. In a second experiment, Ghetti and Mariani (1956) fed rabbits 1000 mg/kg/day naphthalene and reported the development of cataracts between days 3 and 46. Fitzhugh and Buschke (1949) reported that 2% (20,000 ppm) naphthalene in the diets of weanling rats produced slight cataracts in 2 months of treatment.

Optic atrophy and bilateral cataracts were diagnosed in a 36-year-old man during an examination 1 year after he had ingested 5 g (~71 mg/kg, assuming 70 kg body weight) of naphthalene in oil (Lezenius, 1902); he had become nearly blind within 9 hours of ingesting the naphthalene. A 44-year-old man who worked with powdered naphthalene developed cataracts and retinal hemorrhage and a co-worker had chorioretinitis in one eye (Van der Hoeve, 1906). Of workers exposed to naphthalene (fumes or dust) for up to 5

years in a plant manufacturing dye intermediate, 8/21 developed cataracts (Ghetti and Mariana, 1956). Because the workers were <50 years of age, it is unlikely that they would have developed cataracts spontaneously.

U.S. EPA (1980a) reviewed a number of cases of naphthalene poisoning that reported hemolytic anemia with associated jaundice and, occasionally, renal disease (from precipitated hemoglobin) in infants, children and adults. Exposure to naphthalene occurred by ingestion, inhalation and possibly skin contact. Infants suffering from naphthalene-induced acute hemolytic anemia had high levels of bilirubin in their serum, and some had associated brain damage (kernicterus). Harden and Baetjer (1978) reported a case of aplastic anemia in a 68-year-old woman whose occupation for 39 years included the mothproofing of clothing with naphthalene and paradichlorobenzene.

Shopp et al. (1984) and Borzelleca (1983) reported acute oral LD_{50}s of 533 mg/kg in male CD-1 mice and 710 mg/kg in female mice for naphthalene administered in corn oil.

Warren et al. (1982) reported a 24-hour LD_{50} of naphthalene administered intraperitoneally in corn oil to male Swiss Webster mice 380 mg/kg (350-413 mg/kg, 95% confidence limits, n=65).

The acute oral LD_{50}s of naphthalene in peanut oil administered to Sherman rats by gavage were 2200 mg/kg for males (n=40; 1897-2552, 95% confidence limits) and 2400 for females (n=40; 2105-2736, 95% confidence limits) (Gaines, 1969).

Naphthalene has been shown to bind to hemoglobin, although the extent of binding was lower than that exhibited by carcinogenic polycyclic aromatic hydrocarbons (Pereira and Chang, 1981).

5.7. SUMMARY

Knake (1956) reported increased incidence of lymphosarcomas in rats injected with 500 mg/kg coal tar naphthalene every 2 weeks for 7 treatments; however, the injection site was painted with a carcinogen (carbolfuchsin) and the naphthalene was known to contain impurities. In another study, Knake (1956) painted mice with a 0.5% solution of coal tar naphthalene and reported an increased incidence of lymphatic leukemia. Again, the coadministration of carcinogenic impurities cannot be discounted.

Schmahl (1955) observed no tumors in BDI and BDII rats fed naphthalene in doses of 10-20 mg/day, 6 days/week up to a total dose of 10 g/rat for 700 days, or in rats receiving a single intraperitoneal or subcutaneous dose of 20 mg/rat/week for 40 weeks. An increase in the number or size of γ-GT positive foci was not observed in the livers of rats exposed to naphthalene after partial hepatectomy (Tsuda et al., 1980). Naphthalene is currently being tested by the National Toxicology Program, but final results are not available and histopathology is currently in progress (NTP, 1985).

Naphthalene was found to be nonmutagenic in a variety of microsomal/bacterial assay systems (see Table 5-1) (McCann et al., 1975; Seixas et al., 1982; NTP, 1982; Anderson and Styles, 1978; Kaden et al., 1979; Mamber et al., 1983; Sina et al., 1983). Naphthalene was negative for transformation activity and tumorigenicity when tested *in vitro* using rat and mouse cells pretreated with leukemia virus (Freeman et al., 1973; Rhim et al., 1974).

Results of available teratogenicity reports are summarized in Table 5-2 and are somewhat unclear. Matorova and Chetverikova (1981) reported no visible or microscopic anomalies at 0.075 mg/kg, but embryonic and preimplantation mortality was significantly higher and subcutaneous hematomas were observed on the spine and extremities at $\geq$0.15 mg/kg. Plasterer et al.

(1985) reported reduced numbers of live young at parturition, probably because of early embryonic mortality in mice treated during gestation with 300 mg/kg/day. Coworkers at one laboratory (Harris et al., 1979; Hardin et al., 1981) reported both no evidence of fetal or maternal toxicity in the latter publication and progeny with retarded cranial ossification and heart development in the former publication when an intraperitoneal dose of 395 mg/kg naphthalene was given on days 1-15 of gestation to female Sprague-Dawley rats.

Naphthalene or its metabolites apparently can cross the placenta in humans in amounts sufficient to cause fetal toxicity (U.S. EPA, 1980a; Bergheim et al., 1973). Hemolytic anemia has been observed in infants whose mothers were exposed to naphthalene during pregnancy (Zinkham and Childs, 1958; Anziulewicz et al., 1959).

The NTP has investigated the subchronic toxicity of naphthalene in 13 week studies in rats (NTP, 1980a) and mice (NTP, 1980b). In rats, mortality, frank signs of toxicity, lesions in the kidneys and thymus, and signs of anemia occurred at 400 mg/day, mild kidney lesions occurred at 200 mg/kg (lower dose groups were not examined histologically) and body weight gain depression occurred in males at 200 and females at 100 mg/kg. No adverse effects occurred at $\leq$50 mg/kg. In mice, frank but transient signs of toxicity occurred only at 200 mg/kg, the highest dose tested. No signs of toxicity occurred at 100 mg/kg and no compound-related histopathological lesions were observed at 200 mg/kg, the only treatment group histopathologically examined. In both the rat and mice studies, treatments were given 5 days/week.

When naphthalene was administered by gavage to male and female CD-1 mice for 90 days at doses of 5.4, 53 and 133 mg/kg/day, no compound-related mortality or changes in body weights were observed (Shopp et al., 1984). Absolute and relative spleen weights were reduced in female mice at the high dose only, but no changes in organ weights were observed in the males. No compound-related effects were observed on serum enzymes and electrolyte levels or immunological screening tests. There was no evidence of compound-induced hemolytic anemia, cataract formation, lung damage or other pathological effects. A significant decrease in hepatic microsomal aryl hydrocarbon hydroxylase was observed in both sexes.

Schmahl (1955) reported no compound-related effects on mortality, histopathology, tumor formation, eye damage or signs of toxicity in BDI and BDII rats administered naphthalene orally at doses of 10-20 mg/day, 6 days/week from age 100-800 days. The rats were observed until spontaneous death, and the average lifespan was 800 days.

Several short-term animal studies reported cataract development as a result of naphthalene administration (Ghetti and Mariani, 1956; Van Heyningen and Pirie, 1976; Fitzhugh and Buschke, 1949). Naphthalene has been associated with cataract formation (Lezenius, 1902; Ghetti and Mariana, 1956) and anemias (U.S. EPA, 1980a; Harden and Baetjer, 1978) in humans.

6. AQUATIC TOXICITY

A great deal of information is available concerning toxicity of crude oil fractions containing naphthalene to aquatic organisms. Studies in which it is not possible to determine naphthalene concentrations, or attribute observed effects specifically to naphthalene itself, have been omitted from this chapter.

6.1. ACUTE

The available data concerning acute toxicity of naphthalene to fish and amphibians are presented in Table 6-1. The lowest concentrations that were acutely toxic to freshwater fishes were 0.028-0.239 mg/ℓ, which caused 8-35% mortality of largemouth bass, Micropterus salmoides, embryos and larvae relative to controls (Black et al., 1983). The lowest reported LC_{50} value was 0.11 mg/ℓ, which applies to embryo-larval stages of rainbow trout, Salmo gairdneri (Black et al., 1983). Among saltwater species, the lowest reported toxic concentrations were 0.002 mg/ℓ, which caused an increased incidence of gill hyperplasia, and 0.02 mg/ℓ, which caused taste bud necrosis, in mummichogs, Fundulus heteroclitus (DiMichele and Taylor, 1978). The lowest reported LC_{50} value was 1.2 mg/ℓ, the 96-hour LC_{50} for pink salmon, Oncorhynchus gorbuscha, in saltwater (Moles et al., 1981).

Data concerning acute toxicity of naphthalene to invertebrates are presented in Table 6-2. The lowest reported LC_{50} value was 1 mg/ℓ, the 96-hour LC_{50} for dragonfly larvae, Somatochlora singulata (Correa and Coler, 1983) and Daphnia pulex (Trucco et al., 1983). Among saltwater invertebrates, larval crustaceans appear to be the most sensitive organisms, with 0.008-0.012 mg/ℓ causing 100% mortality of spot shrimp, Pandalus platyceros, and dungeness crab, Cancer magister, larvae (Sanborn and Malins, 1977).

TABLE 6-1

Acute Toxicity of Naphthalene to Aquatic Vertebrates

Species	Concentration (mg/L)	Effect	Reference
		FRESHWATER SPECIES	
Coho salmon	0.77	96-hour LC_{50}, parasitized fish	Moles, 1980
Oncorhynchus kisutch	3.22	96-hour LC_{50}, unparasitized fish	Moles, 1980
	11.8	toxic, eggs	Korn and Rice, 1981
	5.6	toxic, emergent fry	Korn and Rice, 1981
	2.1	96-hour LC_{50}	Moles et al., 1981
	5.6	50% mortality, <6 hours	Holland et al., 1960
	3.2-5.6	72-hour critical level	Holland et al., 1960
Rainbow trout	2.3	96-hour LC_{50}	DeGraeve et al., 1980
Salmo gairdneri	1.6	96-hour LC_{50}	DeGraeve et al., 1982
	0.11	LC_{50}, embryo-larval test from fertilization to 4 days post-hatch	Black et al., 1983
	0.12	27-day LC_{50}	Millemann et al., 1984
Mosquito fish	150	96-hour LC_{50}	Wallen et al., 1957
Gambusia affinis			
Fathead minnow	7.9	96-hour LC_{50}	DeGraeve et al., 1982
Pimephales promelas	1.99	96-hour LC_{50}	Millemann et al., 1984
	6.08	96-hour LC_{50}	Holcombe et al., 1984
	4.9	96-hour LC_{50}, 14°	DeGraeve et al., 1980
	8.9	96-hour LC_{50}, 24°	DeGraeve et al., 1980
	>0.44	MATC	U.S. EPA, 1978
Minnows (unspecified)	11-18	lethal, 6 hours	McKee and Wolf, 1963
Largemouth bass	0.51	LC_{50}, embryo-larval test from fertilization to 4 days post-hatch	Black et al., 1983
Micropterus salmoides	0.028-0.239	8-35% mortality	Black et al., 1983
	0.68	7-day LC_{50}	Millemann et al., 1984
Cichlid	7.9	lethal	Dange and Masurekar, 1982
Tilapia mossambica			
Tadpole	2.1	96-hour, LC_{50}	Edmisten and Bantle, 1982
Xenopus laevis	1.7	6-hours, absence of swimming	Edmisten and Bantle, 1982

TABLE 6-1 (cont.)

Species	Concentration (mg/L)	Effect	Reference
		SALTWATER SPECIES	
Mummichog	4-6	lethal	Levitan and Taylor, 1979
Fundulus heteroclitus	≥0.2	histopathological effects on brain, liver, pancreas, 15 days	DiMichele and Taylor, 1978
	0.02	neurosensory damage, increased serum cortisol, glucose, protein, 15 days	DiMichele and Taylor, 1978
	0.002	gill hyperplasia, 15 days	DiMichele and Taylor, 1978
	1.73	lethal, 15 days	Taylor, 1979
	1.60	no effect, 30 days	Taylor, 1979
Sheepshead minnow Cyprinodon variegatus	2.4	24-hour LC_{50}	Anderson et al., 1974
Pink salmon	1.37	96-hour LC_{50}, 4°	Korn et al., 1979
Oncorhynchus gorbuscha	1.84	96-hour LC_{50}, 8°	Korn et al., 1979
	1.24	96-hour LC_{50}, 12°	Korn et al., 1979
	1.2	96-hour LC_{50}	Moles et al., 1981

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TABLE 6-2

Acute Toxicity of Napthalene to Aquatic Invertebrates

Species	Concentration (mg/L)	Effect	Reference
		FRESHWATER SPECIES	
Crustaceans			
Water flea, Daphnia magna	8.57	48-hour LC_{50}	U.S. EPA, 1978; LeBlanc, 1980
	0.6	48-hour NOEC	U.S. EPA, 1978; LeBlanc, 1980
	2.6	48-hour LC_{50}	Millemann et al., 1984
	2.92-3.89	48-hour LC_{50}	Geiger and Buikema, 1982
	22.6	48-hour LC_{50}	Eastmond et al., 1984
	3.4-4.1	48-hour LC_{50}	Crider et al., 1982
Water flea, Daphnia pulex	1	96-hour LC_{50}	Trucco et al., 1983
	3.4	118-hour LC_{50}	Geiger and Buikema, 1981
	0.28-0.68	no effects on oxygen consumption, feeding rate	Geiger and Buikema, 1981
Amphipod, Gammarus minus	3.93	48-hour LC_{50}	Millemann et al., 1984
Insects			
Midge, Chironomus tentans	2.81	48-hour LC_{50}	Millemann et al., 1984
Midge, Chironomus attenatus	5	oxygen consumption inhibited	Crider et al., 1982
Dragonfly, Somatochlora cingulata	2-2.5	96-hour LC_{50}	Correa and Coler, 1983
	0.01-0.10	increased respiration	Correa and Coler, 1983
Mollusks			
Snail, Physa gyrina	5.02	48-hour LC_{50}	Millemann et al., 1984
		SALTWATER SPECIES	
Crustaceans			
Grass shrimp, Palaemonetes pugio	2.35	48-hour LC_{50}	Tatem and Anderson, 1973
	2.6	24-hour LC_{50}	Anderson et al., 1974
Shrimp, Pandalus goniurus	0.97	96-hour LC_{50}, 12°	Korn et al., 1979
	1.02	96-hour LC_{50}, 8°	Korn et al., 1979
	2.16	96-hour LC_{50}, 4°	Korn et al., 1979
Spot shrimp, Pandalus platyceros	0.008-0.012	100% mortality of larvae	Sanborn and Malins, 1977
Brown shrimp, Penaeus aztecus	2.5	96-hour LC_{50}	Tatem et al., 1978
	2.5	24-hour LC_{50}	Anderson et al., 1974
Brine shrimp, Artemia salina	2.11-2.89	EC_{50}, immobilization	Foster and Tullis, 1985

TABLE 6-2 (cont.)

Species	Concentration (mg/L)	Effect	Reference
SALTWATER SPECIES (cont.)			
Crustaceans (cont.)			
Amphipod, Elasmopus pectenicrus	2.68	96-hour LC_{50}	Lee and Nicol, 1978a
Amphipod, Paryhale hawaiensis	6-10	some mortality, 24 hours	Lee and Nicol, 1978b
	3-4	no mortality, 24 hours	Lee and Nicol, 1978b
Mysid, Neomysis americana	1.11	increased oxygen consumption	Smith and Hargreaves, 1984
	0.8-1.4	96-hour LC_{50}	Hargreaues et al., 1982
	0.85	96-hour LC_{50}, 25°	Smith and Hurgreaves, 1983
	1.28	96-hour LC_{50}, 15°	Smith and Hurgreaves, 1983
Blue crab, Callinectes sapidus	2-5	defensive display, locomotor activity	Pearson and Olla, 1980
	10^{-7}	detection limit	Pearson and Olla, 1980
	1.8	increased ventilation and heart rate	Sabourin, 1982
Dungeness crab, Cancer magister	0.008-0.012	100% mortality, larvae	Sanborn and Malins, 1977
	0.01	detection threshold	Pearson et al., 1980
Fiddler crab, Uca minax	2.9	histopathological effects on hepatopancreas, 5 days	Robinson and Dillaman, 1985
Fiddler crab, Uca pugilator	10.69	inhibition of circadian pigment dispersion, 4 days	Staub and Fingerman, 1984
Crab, Scylla serrata	11	lethal to all life stages, 15 days	Kulkarni and Masurekar, 1984
Copepod, Eurytemora affinis	1	decreased fecundity and ingestion rate, 24 hours	Berdugo et al., 1977
	0.01-0.05	no effect feeding and reproduction, 10 days	Berdugo et al., 1977
Mollusks			
Pacific oyster, Crassostrea gigas	199.0	96-hour LC_{50}	LeGore, 1974
European flat oyster, Ostrea edulis	0.0657	stimulated protein and lipid catabolism	Riley and Mix, 1981
Mussel, Mytilus edulis	saturated	decreased respiration	Major, 1977
Worms			
Polychaete, Neanthes arenaceodentata	3.8	96-hour LC_{50}	Rossi and Neff, 1978

6.2. CHRONIC

Results of long-term aquatic toxicity studies with naphthalene are summarized in Table 6-3. The lowest reported toxic concentrations in three studies with freshwater species were in the range of 0.6-0.9 mg/ℓ, and were, therefore, higher than the lowest LC_{50} value, 0.11 mg/ℓ for rainbow trout larvae (Black et al., 1983). No chronic toxicity data for rainbow trout were available, but an embryo-larval test with this sensitive species might reveal lower thresholds for sublethal toxicity.

Of two long-term studies with saltwater, the lowest reported toxic concentration was 0.01 mg/ℓ, which inhibited reproduction and decreased the lifespan of copepods, Eurytemora affinis (Ott et al., 1978).

6.3. PLANTS

Data concerning effects of naphthalene on aquatic plants are presented in Table 6-4. The lowest concentration that caused clearly adverse effects was 0.4 mg/ℓ, which caused a 50% reduction in growth of the saltwater alga, Skeletonema costatum (Oestgaard et al., 1984).

6.4. RESIDUES

Several studies are available concerning uptake and accumulation of naphthalene by aquatic organisms. Data from laboratory uptake experiments are presented in Table 6-5. Many of the reported BCFs were determined in short-term (<1 day) experiments and probably do not represent steady-state values. In some fish and invertebrate species, 1-9 days of exposure is required before naphthalene residues reach a plateau or steady-state level, depending on naphthalene concentration, the species in question and the life stage being exposed (Harris et al., 1977; Korn and Rice, 1981). For example, coho salmon, Onchorhynchus kisutch, alevins and fry achieved maximum tissue concentrations after 36 and 10 hours exposure, respectively.

TABLE 6-3

Chronic Toxicity of Napthalene to Aquatic Organisms

Species	Concentration (mg/l)	Effect	Reference
		FRESHWATER SPECIES	
Fathead minnow *Pimephales promelas*	0.85	growth inhibition, embryo-larval test	DeGraeve et al., 1982
	0.45	NOEC, embryo-larval test	DeGraeve et al., 1982
Coho salmon *Oncorhynchus kisutch*	0.67-1.4	decreased length and weight relative to controls, 40 days	Moles et al., 1981
Water flea *Daphnia pulex*	0.60	decreased growth	Geiger and Buikema, 1982
	0.33	increased lifespan and reproduction	
		SALTWATER SPECIES	
Pink salmon *Oncorhynchus gorbuscha*	0.38-0.80	dose-related depression of body weight gain, 40 days	Moles and Rice, 1983
	0.12	NOEC	Moles and Rice, 1983
Copepod *Eurytemora affinis*	0.01	decreased lifespan, number of offspring, and mean brood size, 29 days (entire lifespan)	Ott et al., 1978

TABLE 6-4

Effects of Naphthalene on Aquatic Plants and Bacteria

Species	Concentration (mg/L)	Effect	Reference
		PLANTS	
Green alga *Selenastrum capricornutum*	2.96	4-hour EC_{50}	Millemann et al., 1984
Diatom *Nitzschia palea*	2.82	4-hour EC_{50}	Millemann et al., 1984
Flagellate *Chlamydomonas angulosa*	34.4 100% sat	61% mortality, 24 hours complete inhibition of photosynthesis	Soto et al., 1975 Hellebust et al., 1982
Green alga *Chlorella vulgaris*	33.0	48-hour EC_{50}, cell numbers	U.S. EPA, 1978
Marine alga *Pavlova lutheri*	0.1	change in motility pattern	Vandermuelen et al., 1983
Marine alga *Skeletonema costatum*	0.4	50% growth reduction	Oestgaard et al., 1984
		BACTERIA	
Serratia marinorubura	5.90 11.03	no effect decreased growth	Calder and Lader, 1976 Calder and Lader, 1976
Vibrio parahaemolyticus	1.41 5.77	no effect decreased growth	Calder and Lader, 1976 Calder and Lader, 1976

TABLE 6-5

Data Concerning Naphthalene Accumulation in Aquatic Organisms

Species	Water Concentration (mg/L)	Duration	Tissue Concentration (mg/g)	BCF	Reference
			FISH		
Bluegill *Lepomis machrochirus*	NA	NA	NA	98	Phipps et al., 1984
Coho salmon *Oncorhynchus kisutch*	NA	3 hours	NA	20-42	Korn and Rice, 1981
Rainbow trout *Salmo gairdneri*	0.005-0.003	4 weeks	NA	40-300	Melancon and Lech, 1978
Sheepshead minnow *Cyprinodon variegatus*	1.0	4 hours	60	60	Anderson et al., 1974
Mummichog *Fundulus heteroclitus*	0.02	4 hours	0.04	2	DiMichele and Taylor, 1978
	2.0	4 hours	4.4	2	DiMichele and Taylor, 1978
Sand goby *Gillichius mirabilis*	NA	1 hour	NA	63	Lee et al., 1972a
Sculpin *Oligocottus maculosus*	NA	3 hours	NA	32	Lee et al., 1972a
Sanddab *Citharichthys stigmaeus*	NA	1 hour	NA	77	Lee et al., 1972a
			INVERTEBRATES		
Water flea *Daphnia magna*	1.8	5 hours	NA	50	Eastmond et al., 1984
Water flea *Daphnia pulex*	NA	24 hours	NA	131	Southworth et al., 1978
	3.24	24 hours	NA	677	Trucco et al., 1983
Copepod *Eurytemora affinis*	0.001	9 days	50*	50,000*	Harris et al., 1977
Copepod *Calanus helgolandicus*	0.0002	24 hours	0.1*	500*	Harris et al., 1977

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TABLE 6-5 (cont.)

Species	Water Concentration (mg/L)	Duration	Tissue Concentration (mg/g)	BCF	Reference
			INVERTEBRATES (cont.)		
Spot shrimp Pandalus platyceros	NA	10 hours	0.82	100	Sanborn and Malins, 1977
Brown shrimp Penaeus aziecus	0.3	30 minutes	0.65	NA	Anderson et al., 1974
Dragonfly Somatochlora cingulata	0.1 0.01	48 hours 48 hours	17.7 15.5	178 1,548	Correa and Coler, 1983 Correa and Coler, 1983
Oyster Crassostrea virginica	NA NA	8 hours 4 days	14.7 6.3	NA NA	Neff et al., 1976
Oyster Ostrea edulis	NA	72 hours	NA	24-62	Riley et al., 1981b
Mussel Mytilus edulis Mytilus edulis Mytilus edulis	 0.032 0.032 NA	 4 hours 76 hours NA	 7 3 NA	 NA NA 31-37	 Lee et al., 1972b Lee et al., 1972b Geyer et al., 1982
Snail Thais lima	NA NA	28 days 14 days	0.43 1.40	75 40	Stickle et al., 1984 Stickle et al., 1984
Clam Rangia cuneata	0.84	24 hours	1.9	2.3	Neff et al., 1976

*Dry weight

NA - Not available

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In contrast, it took 10 days for eggs to reach steady-state (Korn and Rice, 1961). In general, the data in Table 6-5 indicate that naphthalene does not bioaccumulate to a great extent in most species (i.e., most BCF values are <500).

The study by Harris et al. (1977) had the highest naphthalene BCF values. In this study, marine copepods, Eurytemora affinis and Calanus helgolandicus, were exposed to naphthalene in seawater until a steady-state was reached. E. affinis achieved a steady-state concentration of 50 µg/g (dry weight) after 9 days exposure to 1 µg/L, for an apparent BCF value of 50,000. In deriving a more meaningful BCF value from these data, U.S. EPA (1980a) calculated an approximate tissue naphthalene concentration on a wet weight basis and thus arrived at a BCF of 5000. The other copepod, C. helgolandicus, reached a steady-state concentration of 0.11 µg/g dry weight after only 24 hours exposure to 0.2 µg/L, an apparent BCF of ~500. U.S. EPA (1980a) also converted these data to derive a wet weight BCF of 50.

The relative importance of naphthalene uptake from food vs. uptake from water is difficult to assess. Fortner and Sick (1985) found that oysters, Crassostrea virginica, accumulated naphthalene to a greater extent when exposed to it in water rather than food particles. On the other hand, Corner et al. (1976) reported that dietary uptake was more important in the copepod, Calanus helgolandicus. Depuration also occurred more slowly when naphthalene was taken up from the diet rather than water.

Sites of naphthalene accumulation vary in different species. In rainbow trout, skin was found to be a site of significant accumulation, regardless of whether naphthalene was administered in the water, orally or by injection (Varanasi et al., 1978). Collier et al. (1980) reported that naphthalene

also accumulated in the brain of rainbow trout after oral or intravenous administration. In studies with three saltwater fish species, Gillichthys micrabilis, Oligocottus maculosus and Citharichthys stigmaeus, Lee et al. (1972a) found that the liver and gall bladder were sites of naphthalene accumulation. In eggs of coho salmon, naphthalene concentrated primarily in the yolk (Korn and Rice, 1981). In oysters, Ostrea edulis, naphthalene initially accumulated in gills, and then accumulated in the adductor muscle and the body of the organism after a lag period (Riley et al., 1981a).

Naphthalene is apparently metabolized extensively in many aquatic species. Roubal et al. (1977) reported that naphthalene was metabolized to 1-napthol, 1-napthyl glucuronic acid and 1,2-dihydro-1,2-dihydroxynaphthalene by coho salmon. Varanasi et al. (1979) also found that dietary naphthalene was initially metabolized to 1,2-dihydro-1,2-dihydroxynaphthalene in the liver of starry flounder, Platichthys stellatus, and rock sole, Lepidopsetta bilineata. After 24 hours, however, the concentration of this compound in the liver decreased while conjugated forms increased. In a study with English sole, Parophrys vetulus, Reichert and Varanasi (1982) also found that 1,2-dihydro-1,2-dihydroxynaphthalene (diol) was the major nonconjugate metabolite, and glucuronides were the major class of conjugates. Additional data indicated that glucuronide conjugates in the liver were derived from the diol. In the spot shrimp, Pandalus platyceros, naphthalene was metabolized to glucuronide, sulphate, dihydroxydiol and phenolic derivatives (Sanborn and Malins, 1980).

Naphthalene elimination can occur by biliary, renal, epidermal or gill routes (Varanasi et al., 1979). Gills were the primary route of excretion in the dolly varden char, Salvelinus malma (Thomas and Rice, 1981). Naphthalene itself is apparently eliminated rapidly by most species, although

some of its metabolites are eliminated more slowly (Sanborn and Malins, 1977). The elimination half-time for naphthalene in rainbow trout was reported to be <24 hours (Melancon and Lech, 1979). Oysters, Crassostrea virginica, and clams, Rangia cuneata, eliminated >50% of their total body burden in 24 hours in uncontaminated water (Neff et al., 1976). Corner and Harris (1976) found that the copepod Eurtemora affinis also eliminated 50% of its naphthalene in the first 24 hours, but that depuration slowed after that. The copepod, Calanus helgolandicus, exposed to radiolabeled naphthalene, eliminated 80% of its total radioactivity after 5 hours in clean water, but 7% of the radioactivity still remained after 2 weeks (Corner and Harris, 1976). These results suggest a two-stage elimination pattern. Eastmond et al. (1984) reported that it took 0.5 hours for Daphnia magna to eliminate the first 50% of its body burden, but that elimination did not follow first-order kinetics.

Varanasi and Gmur (1981) found that some marine fishes (Pleuronectidae) eliminated naphthalene primarily as glucuronide conjugates in the bile. In contrast, marine invertebrates had a large proportion of sulphate conjugates. Neff (1975) suggested that fish and shrimp possessed enzymatic detoxification mechanisms for naphthalene and thus could eliminate it more rapidly than clams and oysters.

6.5. SUMMARY

The lowest reported LC_{50} values for freshwater and saltwater fishes were 0.11 mg/ℓ for rainbow trout larvae (Black et al., 1983) and 1.2 mg/ℓ for pink salmon (Moles et al., 1981), respectively. The lowest reported LC_{50} value for freshwater invertebrates was 1 mg/ℓ for dragonfly, Somatochlora singulata, larvae (Correa and Coler, 1983) and Daphnia

pulex (Trucco et al., 1983). Among saltwater invertebrates, larval crustaceans appeared to be the most sensitive to naphthalene, with 0.008-0.012 mg/L causing 100% mortality of spot shrimp and dungeness crab larvae (Sanborn and Malins, 1977). Limited chronic and subchronic toxicity data did not indicate lower thresholds for toxicity than the acutely toxic levels in the most sensitive species.

The lowest concentration that caused clearly adverse effects on aquatic plants was 0.4 mg/L, which caused a 50% reduction in growth of the marine alga Skeletonema costatum (Oestgaard et al., 1984).

Data concerning naphthalene residues in aquatic biota indicated that naphthalene does not bioaccumulate to a great extent in most species. In general, naphthalene appeared to be metabolized and eliminated rapidly.

7. EXISTING GUIDELINES AND STANDARDS

7.1. HUMAN

ACGIH (1980, 1984) has recommended a TLV-TWA of 50 mg/m³ (10 ppm) and a STEL of 15 ppm (75 mg/m³) for occupational exposure to naphthalene. Since eye irritation was observed at 15 ppm, this criterion was chosen to "prevent ocular effects but possibly not blood changes in hypersusceptibles" (ACGIH, 1980). The OSHA standard for exposure to naphthalene in the workplace is 10 ppm (50 mg/m³) (CFR, 1981).

The U.S. EPA (1980a) declined to derive an ADI for naphthalene because of the limited available data base.

7.2. AQUATIC

U.S. EPA (1980a) did not derive an ambient water quality criterion for naphthalene for the protection of aquatic life, but did note that acute and chronic toxicity to freshwater species occurred at concentrations as low as 2.3 and 0.62 mg/ℓ, respectively, and would occur at lower concentrations in species more sensitive than those tested. U.S. EPA (1980a) also reported that acute toxicity to saltwater species occurred at concentrations as low as 2.35 mg/ℓ and would occur at lower concentrations in more sensitive species. More recent data (see Chapter 6) suggest that naphthalene concentrations as low as 0.02 mg/ℓ may be toxic to both freshwater and marine species.

8. RISK ASSESSMENT

The National Toxicology Program is currently evaluating napathalene for carcinogenicity by inhalation using mice. Final results are not available; chronic histopathology is currently in progress (NTP, 1985). In the available literature, Knake (1956) reported increased incidences of lymphosarcomas in rats injected with coal-tar naphthalene and an increased incidence of lymphatic leukemia in mice painted with a 0.5% solution of coal-tar naphthalene. The possible coadministration of carcinogenic impurities or the use of an experimental carcinogen (carbolfuchsin) cannot be discounted, however.

Schmahl (1955) observed no tumors in BDI and BDII rats fed naphthalene in doses of 10-20 mg/day, 6 days/week from age 100-800 days. The rats were observed until spontaneous death, which in some cases was >1000 days. Data are insufficient at this time to consider naphthalene a potential carcinogen.

Naphthalene was found to be nonmutagenic in a variety of microsomal/bacterial assay systems (see Table 5-1) (McCann et al, 1975; Seixas et al., 1982; NTP, 1982; Andersen and Styles, 1978; Kaden et al., 1979; Mamber et al., 1983; Sina et al., 1983) and in mammalian test systems (Sina et al., 1983; Freeman et al., 1973; Rhim et al., 1974; Tonelli et al., 1979).

Results of available teratogenicity reports are somewhat unclear (see Table 5-2). Harris et al. (1979) and Hardin et al. (1981) reported no evidence of fetal or maternal toxicity in the latter publication, but progeny with retarded cranial ossification and heart development in the former publication when an intraperitoneal dose of 395 mg/kg naphthalene was given on days 1-15 of gestation to Sprague-Dawley rats. Matorova and Chetverikova (1981) administered naphthalene intragastrically in doses of

70, 0.15 and 0.075 mg/kg to pregnant rats for 19 days. No visible or microscopic anomalies were found in the group given 0.075 mg/kg. At the 70 and 0.15 mg/kg doses, no visible developmental defects were found, but embryonic and preimplantation mortality was significantly higher and subcutaneous hematomas were observed on the spine and extremities. Pregnancies lasted longer (up to 27 days) in the high-dose group when females were allowed to give birth naturally; pups were born with black tails that fell off 6-8 hours later. The credibility of this Russian study is questionable, since dosages and effects in the text were sometimes unclear and not always in agreement with the tabulated data. Plasterer et al. (1985) observed maternal toxicity (mortality and reduced body weight gain) and fetal mortality (reduced number of live young at parturition) in mice intubated with naphthalene at 300 mg/kg/day for 8 consecutive days starting on day 7 of gestation. Naphthalene has been reported to cause fetal toxicity in humans and hemolytic anemia has been observed in infants whose mothers were exposed to naphthalene during pregnancy (U.S. EPA, 1980a; Bergheim et al., 1973; Zinkham and Childs, 1958; Anziulewicz et al., 1959). Exposure levels for these effects were not available.

In the subchronic toxicity study of naphthalene administered by gavage to F344 rats (NTP, 1980a) at doses of 0, 25, 50, 100, 200 and 400 mg/kg/day, 5 days/week for 13 weeks, the expanded dosages for a 7-day week were 0, 18, 36, 71, 143 and 286 mg/kg/day, respectively. Signs of toxicity, such as diarrhea, lethargy, hunched posture, rough coats and a decrease in body weight gain were seen at the high dose (286 mg/kg/day) in both sexes. At 143 mg/kg/day, decreased body weight gain was observed in both sexes and mild renal lesions (2/10 treated vs. 0/10 control) were observed in the males. Histopathological examination was not performed on animals from

lower dose groups. At 71 mg/kg/day, decreased body weight gain was observed in the females. No signs of toxicity were observed at 36 mg/kg/day, which represents a NOEL for rats in this study. In a similar subchronic toxicity study, naphthalene was administered by gavage to B6C3F1 mice at dosages of 0, 12.5, 25, 50, 100 and 200 mg/kg/day, 5 days/week, equivalent to 0, 9, 18, 36, 71 and 143 mg/kg/day, respectively (NTP, 1980b). Overt but transient signs of toxicity, but no hematological or histological changes, occurred at the high dosage (143 mg/kg/day). No signs of toxicity, changes in body weight gain, changes in hematological or histopathological parameters were observed at the next lower dosage of 71 mg/kg/day, which is designated a NOAEL in the experiment. In a subchronic study by Shopp et al. (1984), naphthalene administered by gavage to CD-1 mice resulted in decreased spleen weights in females at dosages of 133 mg/kg/day. No evidence of toxicity was observed at a dosage of 53 mg/kg/day (NOAEL) for 90 days.

Schmahl (1955) reported the only chronic oral toxicity study of naphthalene located in the available literature. Naphthalene was administered orally to BDI and BDII rats at dosages of 10-20 mg/day up to a total of 10 g/rat, 6 days/week in the diet from the ages of 100-800 days. Assuming a body weight of 0.35 kg, the expanded dosage was equivalent to 24.5-50 mg/kg/day for a 7-day week up to a total dosage of 10 g/rat. This results in a TWA dosage of 40.1 mg/kg/day. The treatment resulted in no effect on lifespan, no effect observed upon gross or histological examination and no signs of toxicity.

Since the data available at this time do not indicate that naphthalene is carcinogenic, it is appropriate to derive an RfD (ADI) based on toxicity data.

The TLV of 10 ppm (50 mg/m³) is based on the observation that eye irritation occurs at 15 ppm and on the concern that continuous exposure may result in serious eye damage (ACGIH, 1980). The TLV and STEL (15 ppm) are intended to protect against ocular effects, but possibly not blood changes in hypersusceptible humans (ACGIH, 1980), which may occur at a lower dosage. The subchronic and chronic oral toxicity studies in rats and mice (NTP, 1980a,b; Shopp et al., 1984; Schmahl, 1955) were not included in the documentation for the TLV (ACGIH, 1980). These subchronic and chronic oral studies are a more appropriate basis for the development of an RfD for oral exposure than the TLV because of the uncertainties involved in route-to-route extrapolation. To date, the results of the NTP chronic toxicity and carcinogenicity study are not available; therefore, until further information is available a provisional ADI based on the chronic oral study of Schmahl (1955) and supported by the subchronic NTP (1980a,b) and Shopp et al. (1984) studies is recommended.

The chronic oral rat NOEL of 40.1 mg/kg/day (Schmahl, 1955) is supported by the subchronic oral NOEL of 36 mg/kg/day reported for rats (NTP, 1980a) and is lower than the subchronic oral LOAEL of 71 mg/kg/day reported for rats in the same study (NTP, 1980a). Mice appeared to be less sensitive than rats to naphthalene, with subchronic NOAELS of 53-71 mg/kg/day and some adverse effects appearing at 133-143 mg/kg/day (NTP, 1980b; Shopp et al, 1984). Although these studies have some deficiencies, together they provide an indication of the threshold for toxicity and a NOEL for long-term oral exposure to naphthalene. Dividing the NOEL of 40.1 mg/kg/day by an uncertainty factor of 100 (10 for the extrapolation from animals to humans and 10 to provide additional protection for the most sensitive individuals in the human population) results in an RfD of 0.40 mg/kg/day, or 28.0 mg/day for a

70 kg man. The RfD for naphthalene should continue to be provisional until information can be obtained from the NTP chronic toxicity and carcinogenicity study, and until adequate teratogenicity and reproductive studies are performed.

The CBI files contained no additional data requiring a modification of the RfD and the provisional RfD of 0.40 mg/kg/day remains unchanged.

9. REPORTABLE QUANTITIES

9.1. REPORTABLE QUANTITY (RQ) RANKING BASED ON CHRONIC TOXICITY

The NTP (1985) has tested the chronic toxicity of naphthalene by inhalation exposure in mice, but the results are not currently available. From case reports in humans, the potential effects of naphthalene exposure include acute hemolytic anemia with associated jaundice and occasional renal damage, eye irritation, cataracts and retinal damage (see Section 5.5.) (U.S. EPA, 1980a; Sandmeyer, 1981; ACGIH, 1980). These effects, however, have been observed with acute exposure to the compound. According to Sandmeyer (1981), individuals with congenital erythrocyte glucose-6-phosphate dehydrogenase deficiency are more susceptible to hemolytic anemia upon exposure to naphthalene. Even though these effects have been observed in humans, the exposure was acute and dose-response information was not available; therefore, development of an RQ classification from these data would not be appropriate.

Cataract development in rats and rabbits (Fitzhugh and Buschke, 1949; Ghetti and Mariani, 1956; Van Heyningen and Pirie, 1976) and degeneration of the retina in rabbits (Van Heyningen and Pirie, 1976) have been observed at daily doses of ~1 g/kg. These studies of ocular toxicity in experimental animals were, however, shorter (28-60 days) than the usual criterion of 90 days for a subchronic study, and the dosage used produced changes in the lens and retina as early as day 1 of treatment. Apparently, organs other than the eye were not observed in these studies. The data for ocular toxicity at high doses, therefore, seems inadequate for development of an RQ classification.

Dose-response information is reported in Table 9-1 from subchronic and chronic oral toxicity studies of naphthalene in rats and mice. As seen from Table 9-1 and as discussed in Chapter 5, no severe effects were observed in BDI and BDII rats fed naphthalene at doses of 24.5-50 mg/kg/day from 100-700 days of age (Schmahl, 1955). In the NTP (1980a) study on F344 rats, the high-dose level of 285.7 mg/kg/day appears to be overtly toxic to the animals and kidney lesions were reported in the males at the next lower dosage of 143 mg/kg/day. Absolute and relative spleen weights were changed in female CD-1 mice at a dosage of 133 mg/kg/day (Shopp et al., 1984). The other effect observed that might be scored for an RQ determination is reduction in rate of gain. The lowest dosage at which body weight was decreased in rats (females) was 71 mg/kg/day (NTP, 1980a) and in mice a dose-related but not significant decrease in body weight gain for females was reported (NTP, 1980b). Therefore, the lowest dosage for body weight effects would be 71 mg/kg/day in female rats (NTP, 1980a) (see Table 9-1). Since the effect on the kidneys in male rats at 143 mg/kg/day could be ranked more severely than the change in spleen weights observed in female mice at a comparable dosage (133 mg/kg/day), this effect will be used to determine a CS (Table 9-2). Multiplying the dosage of 143 mg/kg/day by the cube root of the body weight ratio of the rat body weight of 0.31 kg reported in the study to the reference human body weight of 70 kg, and by 70 kg, results in an equivalent human dose of 1644 mg/day. Since the study was subchronic, it is appropriate to divide the equivalent human dose by an uncertainty factor of 10, resulting in a chronic MED of 164.4 mg/kg/day. The MED corresponds to an RV_d of 2.2. The kidney lesions reported (cortical lymphatic infiltration or focal tubular regeneration) warrant an RV_e of 6. Multiplying the RV_d by the RV_e results in a CS of 13.2, which corresponds to an RQ of 1000.

TABLE 9-1

Oral Toxicity Summary for Naphthalene

Species/ Strain	Sex	Number at Start	Average Weight	Vehicle	Purity	Exposure	Transformed Animal Dose	Response	Reference
F344 Rats	M,F	10/dose/ sex	0.31 (M)[a] 0.18 (F)[a]	corn oil	commer- cial	0, 25, 50, 100, 200 or 400 mg/ kg/day, 5 days/ week, 13 weeks	0, 18, 36, 71, 143, 286 mg/kg/day	At 400 mg/kg, 2 males died at week 1; all high-dose rats had diarrhea, lethargy, hunched posture and rough coats. Significant decrease in body weight gain in both sexes at 400 and 200 mg doses and in females at 100 mg. Both sexes at 400 mg dose had decreases in hemoglobin and hemato- crit. In males, kidney lesions 2/10 at 200 mg and 1/10 at 400 mg, 0/10 in controls. In females, thymus lesions 2/10 at 400 mg, none at 200 mg or controls. No eye lesions ob- served at any dose; no histopathology performed at doses <200 mg/kg.	NTP, 1980a
B6C3F1 Mice	M,F	10/dose/ sex	0.031 kg (M)[a] 0.024 kg (F)[a]	corn oil	commer- cial	0, 12.5, 25, 50, 100, 200 mg/kg/day, 5 days/week, 13/weeks	0, 8.9, 18, 36, 71, 143 mg/kg/day	At high dose, 3-5 weeks -- lethargy, rough haircoats, decreased food con- sumption. All dosed male mice gained more weight than controls. Dose- related nonsignificant decrease in body weight gain in females. No compound-related hematological effects in any group or histopatho- logical effects high-dose group. No eye lesions in any group.	NTP, 1980b
CD-1 Mice	M,F	40-76 (F) 76-112 (M)	0.03 kg[b]	corn oil	commer- cial 99.3%	0, 5.3, 53, 133 mg/kg/day, 90 days	0, 5.3, 53, 133 mg/kg/day	No effects on mortality, body weight, immunological tests, hematology, serum enzyme or electrolyte levels, or organ weights in males. Absolute and relative spleen weights in females reduced at 133 mg dosage. Significant dose-related inhibition of aryl-hydrocarbon hydroxylase activity in males and females.	Shopp et al., 1984
BDI, BDII Rats	NR	28	adult (0.35 kg)[b]	oil	NR	10-20 mg/day, 6 days/week total dose 10 g/rat over 700 days	40.1 mg/kg/day	No effect on mortality, no compound- related histopathology, no tumors, no eye damage, no other signs of toxicity reported.	Schmahl, 1955

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TABLE 9-1 (cont.)

Species/ Strain	Sex	Number at Start	Average Weight	Vehicle	Purity	Exposure	Transformed Animal Dose	Response	Reference
Rabbits (albino and pigmented)	NR	16 dutch 12 albino	adult	NR	NR	1 g/kg for up to 28 days	1 g/kg/day	Cataract development in both strains. Results variable and severity appears not to be related to frequency or duration of dose.	Van Heyningen and Pirie, 1976

[a]Values obtained from weight curves reported in the study

[b]Reference values for body weights (U.S. EPA, 1988b)

NR = Not reported

TABLE 9-1 (cont.)

Species/ Strain	Sex	Number at Start	Average Weight	Vehicle	Purity	Exposure	Transformed Animal Dose	Response	Reference
Rabbits (albino and pigmented)	NR	16 dutch 12 albino	adult	NR	NR	1 g/kg for up to 20 days	1 g/kg/day	Cataract development in both strains. Results variable and severity appears not to be related to frequency or duration of dose.	Van Heyningen and Pirie, 1976

[a]Values obtained from weight curves reported in the study

[b]Reference values for body weights (U.S. EPA, 1988b)

NR = Not reported

TABLE 9-2

Oral Composite Scores for Toxicity of Naphthalene in F344 Rats[a]

Sex	Dose (mg/kg/day)	Human Med[b] (mg/day)	RV_d	Effect	RV_e	CS	RQ
M	143	164.4	2.2	Renal lesions-focal cortical lymphocytic infiltration or focal tubular regeneration	6	13.2	1000
F	71	68.1	2.8	Dose-related decrease in body weight of females.	4	11.2	1000

[a]Source: NTP, 1980a

[b]An uncertainty factor of 10 is applied to the animal dose to expand from subchronic to chronic exposure.

Since body weight changes were observed in rats (NTP, 1980a) (see Table 9-1) at a slightly lower dose (71 mg/kg/day), a CS for this effect was also reported in Table 9-2. Multiplying the dose of 71 mg/kg/day by the cube root of the body weight ratio of the female rat weight (0.18 kg in this study) to the reference human body weight of 70 kg, and by 70 kg, results in an equivalent human dose of 681 mg/day. Since the exposure was subchronic, it is appropriate to divide the equivalent human dose by 10, which results in a chronic MED of 68.1 mg/day (see Table 9-2). The MED corresponds to an RV_d of 2.8. The effect of rate of body weight gain change is given an RV_e of 4. Multiplying the RV_d by the RV_e results in a CS of 11.2, which corresponds to an RQ of 1000.

Examination of Table 9-2 reveals that the CSs derived from the mild histopathological effects on the kidney in males and the reduction in rate of body weight gain in females (NTP, 1980a,b) both correspond to an RQ of 1000; however, the CS for effect in the kidney is higher than that for reduced rate in body weight gain. Therefore, the CS of 13.2 associated with mild renal lesions in male rats (NTP, 1980a) is recommended as the basis for the RQ of naphthalene (Table 9-3). This RQ should be reevaluated when results of the NTP (1985) chronic toxicity study become available.

The U.S. EPA (1983) declined to derive an RQ for naphthalene based on chronic toxicity. The NTP (1980a,b) subchronic studies in rats and mice were not reviewed in this document.

9.2. WEIGHT OF EVIDENCE AND POTENCY FACTOR ($F=1/ED_{10}$) FOR CARCINOGENICITY

Naphthalene is currently being evaluated for carcinogenicity in mice by inhalation by the NTP. Final results are not available, but chronic histopathology is currently in progress (NTP, 1985).

TABLE 9-3

NAPHTHALENE

Minimum Effective Dose (MED) and Reportable Quantity (RQ)

Route:	gavage
Dose*:	164.4 mg/day
Effect:	mild histopathological lesions in the kidney of male rats
Reference:	NTP, 1980a
RV_d:	2.2
RV_e:	6
Composite Score:	13.2
RQ:	1000

*Equivalent human dose

No tumors were reported in the only available oral chronic study. Schmahl (1955) administered naphthalene orally to BDI and BDII rats in doses of 10-20 mg/day, 6 days/week (equivalent to 24.5-50.0 mg/kg/day for a 7-day exposure, assuming a body weight of 0.35 kg) from the age of 100-800 days. Based on the subchronic gavage experiment in rats performed by NTP (1980a), it seems unlikely that the MTD had been approached in this study. No other pertinent carcinogenicity studies reporting dose-related effects in animals or humans were located in the available literature. Therefore, pending the results of the NTP (1985) study of naphthalene, no potency factor can be derived.

Since data are insufficient at this time to access the carcinogenic potential for naphthalene, this compound can be classified as a Group 3 chemical by the IARC classification scheme and in U.S. EPA Group D (i.e., it cannot be classified as to its carcinogenicity to humans) (U.S. EPA, 1984).

10. REFERENCES

ACGIH (American Conference of Governmental Industrial Hygienists). 1980. TLVs: Documentation of Threshold Limit Values, 4th ed. (Includes Supplemental Documentation through 1984). Cincinnati, OH. p. 293.

ACGIH (American Conference of Governmental Industrial Hygienists). 1984. Threshold Limit Values for Chemical Substances and Physical Agents in the Workroom Environment with Intended Changes for 1984-1985. Cincinnati, OH.

Afolabi, O.A., A. Adesulu and O.L. Oke. 1983. Polynuclear aromatic hydrocarbons in some nigerian preserved freshwater fish species. J. Agric. Food Chem. 31: 1083-1090.

Amoore, J.E. and E. Hautala. 1983. Odor as an aid to chemical safety: Odor thresholds compared with threshold limit values and volatilities for 2/4 industrial chemicals in air and water dilution. J. Appl. Toxicol. 3: 272-290.

Anderson, D. and J.A. Styles. 1978. An evaluation of 6 short-term tests for detecting organic chemical carcinogens. Appendix 2. The bacterial mutation test. Br. J. Cancer. 37: 924-930.

Anderson, J.W., J.M. Neff, B.A. Cox, H.E. Tatam and G.M. Hightower. 1974. The effects of oil on estuarine animals: Toxicity, uptake and depuration, respiration. In: Pollution and Physiology of Marine Organisms, F.J. Vernberg and W.B. Vernberg, Ed. Academic Press, Inc., New York. p. 285-310.

Anziulewicz, J.A., et al. 1959. Transplacental naphthalene poisoning. Am. J. Obstet. Gynecol. 78: 519. (Cited in U.S. EPA, 1980a)

Atkinson, R., S. Aschmann and J.N. Pitts, Jr. 1984a. Kinetics of the reactions of naphthalene and biphenyl with HO• and with 03 at 294K. Environ. Sci. Technol. 18: 110-113.

Atkinson, R., C.N. Plum, W.P.L. Carter, A.M. Winer and J.N. Pitts, Jr. 1984b. Rate constants for the gas-phase reactions of nitrate radicals with a series of organics in air at 298K. J. Phys. Chem. 88: 1210-1215.

Bauer, J.E. and D.G. Capone. 1985. Degradation and mineralization of the polycyclic aromatic hydrocarbons anthracene and naphthalene in intertidal marine sediments. Appl. Environ. Microbiol. 50(1): 81-90.

Bedient, P.B., A.C. Rodgers, T.C. Bouvette, M.B. Tomson and T.H. Wang. 1984. Groundwater quality at a creosote waste site. Groundwater. 22: 318-329.

Benoit, F.M., G.L. Lebel and D.T. Williams. 1979. The determination of polycyclic aromatic hydrocarbons at the NG/L level in Ottawa tap water. Int. J. Environ. Anal. Chem. 6: 277-287.

Berdugo, V., R.P. Harris and S.C. O'Hara. 1977. The effect of petroleum hydrocarbons on reproduction of an estuarine planktonic copepod in laboratory cultures. Mar. Pollut. Bull. 8(6): 138-143.

Bergheim, P., G.H. Rathgen and K.J. Netter. 1973. Interaction of drugs and steroids with human placental microsomes. Biochem. Pharmacol. 22(13): 1633-1645.

Bhosle, N.B. and S. Mavinkurve. 1980. Hydrocarbon-utilizing microorganisms from Dona Paula Bay, GOA. Mar. Environ. Res. 4: 53-58.

Bjoerseth, A., O Bjoerseth and P.E. Fjeldstad. 1978. Polycyclic aromatic hydrocarbons in the work atmosphere. I. Determination in an aluminum reduction plant. Scand. J. Work Environ. Health. 4: 212-223.

Black, J.A., W.J. Birge, A.G. Westerman and P.C. Francis. 1983. Comparative aquatic toxicology of aromatic hydrocarbons. Fund. Appl. Toxicol. 3(5): 353-358.

Bogdat'eva, A.G. and D.Y. Bid. 1955. Effect of high molecular weight products of pyrolysis of petroleum on the animal organisms. Gig. Sanit. 7: 21.

Borzelleca, J.F. 1983. A review of volatile organic contaminant data. Proc. AWWA Water Qual. Technol. Conf. p. 225-244.

Bouwer, E.J., P.L. McCarty, H. Bouwer and R.C. Rice. 1984. Organic contaminant behavior during rapid infiltration of secondary wastewater at the Phoenix 23rd Avenue Project. Water Res. 18: 463-472.

Boyd, D.R., et al. 1972. Rearrangement of (1-H^2) and (2-H^2) naphthalene-1,2-oxides to 1-naphthol. Mechanism of the NIH shift. Biochem. J. 11: 1961. (Cited in U.S. EPA, 1980a)

Boyland, E., et al. 1964. Further experiments on implantation of materials into the urinary bladder of mice. Br. J. Cancer. 18: 575. (Cited in U.S. EPA, 1980a)

Brodzinsky, R. and H.B. Singh. 1982. Volatile organic chemicals in the atmosphere: An assessment of available data. Final report on contract 68-02-3452. Environmental Sciences Research Laboratory, Office of Research and Development, U.S. EPA, Research Triangle Park, NC.

Buckpitt, A.R. 1982. Comparative biochemistry and metabolism. Part II: Naphthalene lung toxicity. Air Force Aerosp. Med. Res. Lab. [Tech. Rep.] AFAMRL-TR-82-52. p. 44.

Buckpitt, A.R. 1983. Comparative biochemistry and metabolism. Part II: Naphthalene lung toxicity. Air Force Aerosp. Med. Res. Lab. [Tech. Rep.] AFAMRL-TR-82-52. p. 42.

Buckpitt, A.R. and D.L. Warren. 1983. Evidence of hepatic formation, export and covalent binding of reactive naphthalene metabolites in extrahepatic tissues *in vivo*. J. Pharmacol. Exp. Ther. 225(1): 8-16.

Buckpitt, A.R., L.S. Bahnson and R.B. Franklin. 1985. Evidence that 1-naphthol is not an obligate intermediate in the covalent binding and the pulmonary bronchiolar necrosis by naphthalene. Biochem. Biophys. Res. Commun. 126(3): 1097-1103.

Bull, R.J., J.M. Brown, E.A. Meierhenry, T.A. Jorgenson, M. Robinson and J.A. Stober. 1986. Enhancement of the hepatotoxicity of chloroform in female B6C3F1 mice by corn oil. Implications for chloroform carcinogenesis. Environ. Health Perspect. (In press)

Calder, J.A. and J.H. Lader. 1976. Effect of dissolved aromatic hydrocarbons on the growth of marine bacteria in batch culture. Appl. Environ. Microbiol. 32(1): 95-101.

Callahan, M.A., D.J. Ehreth and P.L. Lenins. 1979. Sources of toxic pollutants found in influent to sewage treatment plants. Proc. Natl. Conf. Munic. Sludge Manage. 8: 55-61.

Carter, W.P.L., A.M. Winer and J.N. Pitts, Jr. 1981. Major atmospheric sink for phenol and cresols. Reaction with nitrate radical. Environ. Sci. Technol. 15: 829-831.

Cerniglia, C.E. and D.T. Gibson. 1977. Metabolism of naphthalene by Cunninghamella elegans. Appl. Environ. Microbiol. 34: 363.

Cerniglia, C.E., D.T. Gibson and C. Vanbaalen. 1979. Algal oxidation of aromatic hydrocarbons: Formation of 1-naphthol from naphthalene by Agmenellum quadruplicatum, Strain PR-6. Biochem. Biophys. Res. Commun. 88: 50-58.

Cerniglia, C.E., D.T. Gibson and C. Vanbaalen. 1980a. Oxidation of naphthalene by cyanobacteria and microalgae. J. Gen. Microbiol. 116: 495-500.

Cerniglia, C.E., R.H. Dodge and D.T. Gibson. 1980b. Studies on the fungal oxidation of polycyclic aromatic hydrocarbons. Bot. Mar. 23: 121-124.

Cerniglia, C.E., J.P. Freeman and R.K. Mitchum. 1982. Glucuronide and sulfate conjugation in the fungal metabolism of aromatic hydrocarbons. Appl. Environ. Microbiol. 43: 1070.

CFR (Code of Federal Regulations). 1981. OSHA Safety and Health Standards 29CFR. 1910.1000.

Chen K.C. and H.W. Dorough. 1979. Glutathione and mercapturic acid conjugations in the metabolism of naphthalene and 1-naphthyl-N-methylcarbamate (carbaryl). Drug Chem. Toxicol. 2(4): 331-354.

Chusid, E. and C.T. Fried. 1955. Acute hemolytic anemia due to naphthalene ingestion. Am. J. Dis. Child. 89: 612. (Cited in U.S. EPA, 1980a)

Cole, R.H., R.E. Fedrick, R.P. Healey and R.G. Rolar. 1984. Preliminary findings of the priority pollutant monitoring project of the nationwide urban runoff program. J. Water Pollut. Control Fed. 56: 898-908.

Collier, T.K., M.M. Krahn and D.C. Malins. 1980. The disposition of naphthalene and its metabolites in the brain of rainbow trout (Salmo gairdneri). Environ. Res. 23: 35-41.

Cooney, J.J., S.A. Silver and E.A. Beck. 1985. Factors influencing hydrocarbon degradation in three freshwater lakes. Microl. Ecol. 11: 127-137.

Corner, E.D.S. and R.P. Harris. 1976. Hydrocarbons in marine zooplankton and fish. Part I. Zooplankton. Soc. Exp. Biol. Semin. Ser. 2(Eff. Pollut. Aquat. Org.). 71(85): 101-105.

Corner, E.D.S., R.P. Harris, C.C. Kilvington and S.C.M. O'Hara. 1976. Petroleum compounds in the marine food web: Short-term experiments on the fate of naphthalene in Calanus. J. Mar. Biol. Assoc. U.K. 56(1): 121-133.

Correa, M. and R. Coler. 1983. Enhanced oxygen uptake rates in dragonfly nymphs (Somatochlora cingulata) as an indication of stress from naphthalene. Bull. Environ. Contam. Toxicol. 30: 269-276.

Crider, J.Y., et al. 1982. Effects of naphthalene on this hemoglobin concentration and oxygen uptake of Daphnia magna. Bull. Environ. Contam. Toxicol. 28: 52-57.

Cupitt, L.T. 1980. Fate of toxic and hazardous materials in the air environment. Environmental Sciences Research Laboratory, Office of Research and Development, U.S. EPA, Research Triangle Park, NC. EPA-600/3-80-084. NTIS PB 80-221948.

Dange, A.D. and V.B. Masurekar. 1982. Naphthalene-induced changes in carbohydrate metabolism in Sarotherodon mossambicus Peters (Pisces:Cichlidae). Hydrobiologia. 94(2): 163-172.

Dean-Raymond, D. and R. Bartha. 1975. Biodegradation of some polynuclear aromatic petroleum components by marine bacteria. Dev. Ind. Microbiol. 16: 97-110.

DeGraeve, G.M., et al. 1980. Effects of naphthalene and benzene on fathead minnows and rainbow trout. Submitted to Trans. Am. Fish. Soc. (Cited in U.S. EPA, 1980)

DeGraeve, G.M., R.G. Elder, D.C. Woods and H.L. Bergman. 1982. Effects of naphthalene and benzene on fathead minnows and rainbow trout. Arch. Environ. Contam. Toxicol. 11(4): 487-490.

Delaune, R.D., G.A. Hambrick and W.H. Patrick, Jr. 1980. Degradation of hydrocarbons in oxidized and reduced sediments. Mar. Pollut. Bull. 11: 103-106.

DiMichele, L. and M.H. Taylor. 1978. Histopathological and physiological responses of Fundulus heteroclitus to naphthalene exposure. J. Fish. Res. Board Can. 35(8): 1060-1066.

Doull, J. 1980. Factors influencing toxicology. In: Casarett and Doull's Toxicology: The Basic Science of Poisons, J. Doull, C.D. Klassen and M.O. Amdurs, Ed. MacMillan Publishing Co., New York, NY. p. 70-83.

Eastmond, D.A., G.M. Booth and M.L. Lee. 1984. Toxicity accumulation, and elimination of polycyclic aromatic sulfur heterocycles in Daphnia magna. Arch. Environ. Contam. Toxicol. 13(1): 105-111.

Edmisten, G.E. and J.A. Bantle. 1982. Use of Xenopus laevis larvae in 96-hour, flowthrough toxicity tests with naphthalene. Bull. Environ. Contam. Toxicol. 29: 392-399.

Ehrlich, G.G., D.F. Goerlitz, E.M. Godsy and M.F. Hult. 1982. Degradation of phenolic contaminants in groundwater by anaerobic bacteria: St. Louis Park, Minnesota. Groundwater. 20: 703-710.

Eiceman, G.A. and V.J. Vandiver. 1983. Adsorption of polycyclic aromatic hydrocarbons on fly ash from a municipal incinerator and a coal-fired power plant. Atmos. Environ. 17(3): 461-465.

Eisele, G.R. 1985. Naphthalene distribution in tissues of laying pullets, swine, and dairy cattle. Bull. Environ. Contam. Toxicol. 34(4): 549-556.

Fazio, T. and J.W. Howard. 1983. Polycyclic aromatic hydrocarbons in foods. In: Handbook of Polycyclic Aromatic Hydrocarbons, A.B. Jorseth, Ed. Marcel Dekker Inc., New York, NY. p. 461-505.

Fedorak, P.M., K.M. Semple and D.W.S. Westlake. 1984. Oil-degrading capabilities of yeasts and fungi isolated from coastal marine environments. Can. J. Microbiol. 30(5): 565-571.